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Formulation of Self Nano-Emulsifying Drug Delivery System (SNEDDS) Loaded Red Fruit Oil (*Pandanus conoideus* Lamk.) using Biodegradable Nutraceutical Surfactant

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Abstract. One of the plants that produce the antioxidant effect is the Red Fruit (Pandanus conoideus Lamk.) and Red fruit oil has low solubility. To overcome this problem, red fruit oil is formulated become SNEDDS with the ratio of red fruit oil, propylene glycol, tween 20, and additional sucrose monoesterpalmitate as a biodegradable surfactant for nutraceuticals, so that it is easily dispersed and covered the oil flavor. The SNEDDS were prepared by nanophase emulsification technique, Particle Size Analyzer to determine the mean zeta potential, Polydispersity Index, and particle size with the comparison between red fruit oil and the combination of surfactant and co-surfactant. The results of SNEDDS from red fruit oil with the good particle size is 227.5 ± 0.42 nm, with ratio oil:surfactant:co-surfactant (25:51.67:23.33), zeta potential value show -54.6 ± 0.17, and Polydispersity Index value show 0.39 ± 0.04. Particle size test results from four formulas, it was found that the greater the concentration of surfactant used, the smaller the particle size. That makes the formulation SNEDDS solubility of red fruit oil can be increased.

1. Introduction

Pharmaceutical formulation technology and drug delivery systems are in the process of discovering a new public pharmaceutical drug which has an advantage of being able to penetrate intercellular spaces only permeable by colloidal particle size [1]. The delivery of nanoparticles is described as the formulation of a dispersed particle at a nanometer or per thousand microns scale and thus it is generally agreed that nanoparticles are particles of a size below 1 micron [2]. Nano particles are the newest drug delivery systems which can increase the delivery rate of drugs to receptors [3]. In the development of drug delivery system based on pharmaceutical technology, a formulation that can improve the ability of active compounds to penetrate is needed, one of them is the Self Nano-Emulsifying Drug Delivery System [4]. Some of the potential advantages of SNEDDS include having the ability to deliver the drug in a dissolved form in the gastrointestinal (GI) tract lumen, thus providing a larger interface area for drug absorption [5]. Nanoemulsion is a transparent, translucent emulsion system and is a water oil dispersion stabilized by a film coating of a surfactant or surfactant molecule, having a droplet size of 50 nm - 500 nm [6].

A type of medicinal plant that can be efficacious as treatment is the red fruit. Red fruit (Pandanus conoideus Lamk.) is an indigenous plant of Papua Province, Indonesia and Papua New Guinea [7]. Red fruit has potential as a functional food because of its carotenoid compounds that are beneficial to health [8]. Carotenoids have several biological activities, such as provitamin A activity, antioxidant activity, protection against the risk of ultraviolet light, regulation of immune function, cell regulation

and proliferation. The beta carotene compound is the main carotenoid which contains provitamin A that is used for vision, tissue differentiation, reproduction, and immunity [9]. The content of red fruit includes fatty acids, tocopherol, beta carotene, and carotenoid [10].

Sugar monoester palmitate is a nonionic surfactant containing sucrose as a hydrophilic group and fatty acid as a lipophilic group that is being developed in the manufacture of nanoparticles. Sugar ester is odorless, tasteless, non-toxic and does not irritate the skin, so it can be used in the manufacture of foods, medicines, cosmetics and other pharmaceutical products. The monoester sucrose has a large emulsion capacity, in which the emulsifiable phase can be emulsified more than any other emulsifier. Based on these advantages, the development of SNEDDS with red fruit oil as the oil phase and Sugar ester as a surfactant is expected to provide better stability [11]. Based on a mixture of nonionic surfactants to enhance oral bioavailability [12]. Experiments were conducted with a variation of surfactant tween 20 which aimed to find out the best surfactant concentration in order to produce a clear microemulsion preparation. In the previous study, tween 20 can be used to make a transparent and stable microemulsion preparation [13]. Previous research was related to the preparation of microemulsion of red fruit oil based on tween differences which resulted in a good solubility for the preparation of microemulsions [14]. This research, we formulated surfactants with red fruit oil to SNEDDS preparations using a Sugar monoester palmitate and tween 20 surfactant ratio.

By doing various studies of the journals and research we have done related to the study of red fruit oil for the preparation of SNEDDS no one has done related to the research so we use the formulation of red fruit oil for the manufacture of SNEDDS with the comparison of a biodegradable nutraceutical surfactant. In this research, adding combination of sugar ester surfactant, kosolven propylene glycol and tween 20 is done in an effort to increase the solubility of red fruit oil in the solubilization preparation. The adding combination of sugar ester surfactant, propylene glycol co-surfactant and tween 20 is expected to increase the solubility of red fruit oil and to see which concentration of surfactant and cosolvent combination can give optimum solubility, so this may increase the absorption of red fruit oil in the preperation form of SNEDDS.

2. Preparation of SNEDDS

2.1 Materials

Red fruit oil (CV Made Mulya Asih), tween 20 (Gatefosse, French propylene glycol (Gatefosse, France), and sucrose monoesterpalmitate (P-1670 Ryoto® Japan) and All ingredients used are available at Pharmaceutical Technology Laboratory Universitas Islam Indonesia

2.2 Method

This study began with a working sequence of manufacturing SNEDDS using SME, PG, Tween 20 and red fruit oil. The solubility of red fruit oil in different oils, surfactants, and cosurfactants is determined in the way the oil phase screening is prepared based on the potential phase of its emulsifying capability. The preparation of red fruit oil SNEDDS done by mixing the red fruit formulation into the surfactant and the cosurfactant can be seen in the formulation table. Then the particle size determination, zeta potential determination, and Polydispersity Index are tested. The formulation can be seen in table 1 and the work scheme can be seen in figure 1.

Table 1. Formulation of Red Fruit Oil

Formulasi	Sucfactant SME + Tween (%)	Co-surfactant PG (%)	Red Fruit Oil (%)
I	41.67	33.33	25
II	45.00	30.00	25
III	48.33	26,67	25
IV	51.67	23.33	25

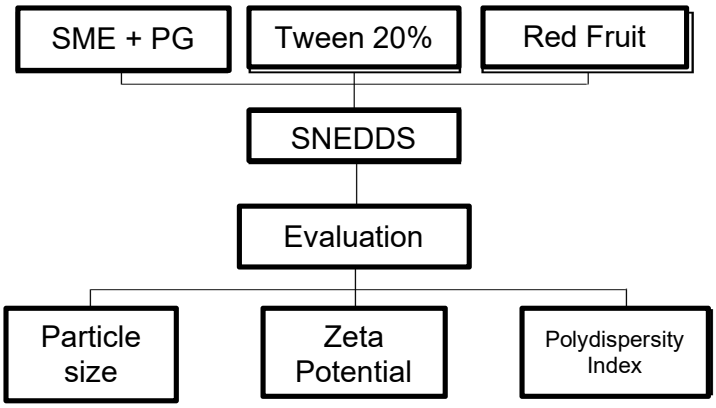

Fig. 1. Work scheme of SNEDDS red fruit oil

2.3 Evaluation of SNEDDS

Determination of particle size, zeta potential, and Polydispersity Index was performed using Particle Size Analysis (PSA). The results can be seen in table 2.

Table 2. Particle size, zeta potential, and polydispersity Index of optimized SNEDDS formulation during storage

Formulation	Particle Size mean ± SD (nm)[a]	Zeta Potential mean ± SD[a]	Polydispersity Index mean ± SD[a]
I	351.8 ± 10.04	-59.85 ± 0.32	0.551 ± 0.23
II	295.45 ± 3.46	-57.70 ± 0.14	0.394 ± 0.12
III	275.35 ± 1.62	-54.25 ± 0.07	0.554 ± 0.20
IV	227.50 ± 0.42	-54.60 ± 0.17	0.399 ± 0.04

[a] Mean ± SD, n = 3

Self Nano-Emulsifying Drug Delivery System (SNEDDS) from red fruit oil with the good particle size is 227.5 ± 0.42 nm, with ratio oil: surfactant:co-surfactant (25:51.67:23.33), zeta potential value show -54.6 ± 0.17, and Polydispersity Index value show 0.39 ± 0.04.

3. Disccusion

Potential Zeta is a scientific term for potential electro kinetics in a colloidal system, potential zeta is the potential difference between the surface layers of strongly bonded ions on the surface of the solid and the electroneutral part of the solution [15]. High electrical charges on the nanoparticles' surface will prevent the aggregation of the nanoparticles due to the strong repulsive force between

particles. The zeta potential value was -54.6 ± 0.17. As a rule of thumb, potential zeta values ± 30 mV will provide good stability and ± 60 mV have excellent stability [16].

This is because tween 20 and propylene glycol have lower molecular weight and viscosity and simpler structure than tween 80 and PEG 400, so it can more easily interact with extract content. The content of extracts that may interact with SMEDDS is the free hydroxyl and oxygen groups, the greater the number of free hydroxyl and oxygen groups in each component allow for the formation of more hydrogen bonds so that the extract is more soluble [17]. Tween 20 is a liquid like yellow oil, distinctive smell, and warm with a bitter taste. tween 20 is a non-anodic hydrophilic surfactant used to make stable aqueous oil emulsions, as a tabulation agent for various substances such as vitamins, and as a bleaching agent in oral formulations, and parenteral suspension [18]. The particle size value was 227.5 ± 0.42 nm because in this study we formulated surfactants with red fruit oil to SNEDDS preparations using a surfactant ratio of Sugar monoester palmitate and tween 20. Surfactant combinations which can provide optimum solubility thus increasee the absorption of red fruit oil in SNEDDS dosage forms.

The polydispersity index is a measure of the mass distribution of molecules in a particular sample. This value shows the result of the calculation of the average weight of the molecule divided by the average number of molecular weights. The closer to zero means the better the distribution. The best polydispersity index produced by the formula I-IV is 0.551 ± 0.23; 0.394 ± 0.12; 0.554 ± 0.20; 0.399 ± 0.04. The fourth PDI value of this formula falls within the middle range of the polydispersity index of 0.08-0.7, this is the upper range in which the distribution algorithm operates best [19].

4. Conclusion

This study developed a simple, fast, and accurate SNEDDS method. The result of SNEDDS from red fruit oil with a good particle size was 227.5 ± 0.42 nm, with a ratio of oil:surfactant:co-surfactant of 25:51.67:23.33, zeta potential value was -54.6 ± 0.17, and Polydispersity Index value was 0.39 ± 0.04. The result of particle size testing using four formulas was the greater the concentration of surfactant used, the smaller the particle size. This meant that tween 20 and Sugar monoester palmitate as a surfactant which is odorless, tasteless, non-toxic and does not irritate the skin, can be used in the manufacturing of food, medicines, cosmetics and other pharmaceutical products.

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