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Research Article

Study of Self Nano-Emulsifying Drug Delivery System (SNEDDS) Loaded Red Fruit Oil (*Pandanus conoideus* Lamk.) As an Eliminated Cancer Cell MCF-7

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ABSTRACT

Red fruit (*Pandanus conoideus* Lamk.) is one of the typical Indonesian plants effective in therapy the breast cancer. This study aimed to preparation and characterization of MCF-7 breast cancer cell test in Self-Nano Emulsifying Drug Delivery System (SNEDDS) loading red fruits. Emulsification technique prepared SNEDDS of red fruits with the ratio of red fruit oil, sugar monoester palmitate, propylene glycol and tween 20 and followed by characterization of MCF-7 breast cancer cell test. SNEDDS obtained was measured by the particle size and tested for breast cancer cells to obtain IC_{50}. The result showed that the optimal ratio oil, surfactant and co-surfactant are 10: 62.5: 17.5) with 193.1 ± 1.68 nm of the particle size, 0.50 ± 0.01 of poly dispersion index, -43.26 ± 0.11 mV of zeta potential and 53.76 ± 0.01 of the transmittance. The determination of breast cell test MFC-7 showed 85.20 µg/mL of IC_{50}. It can be concluded that red fruit in SNEDDS formulation useful in therapy breast cancer with the IC_{50} parameter.

Keywords: breast cancer, MCF-7, red fruit, SNEDDS, sucrose monoester palmitate.

INTRODUCTION

Cancer is a disease that has uncontrolled cleavage characterization so that the growth of a tumour spreads to other distant tissues[1]. Cancer is one of the leading causes of death worldwide. In 2012, about 8.2 million deaths were caused by cancer[2]. Breast cancer is a cause of death is quite high for women in the world[3]. In Indonesia, medicinal herbs have been widely used as self-medication efforts. One type of medicinal plant that can be efficacious as a treatment is red fruit (*Pandanus conoideus* Lamk.) native plants from Papua Province, Indonesia and Papua New Guinea, one of the fruits that contain high antioxidants. Red fruit has potential as a functional food because of carotenoid compounds that are beneficial to health[4]. Carotenoids have several biological activities, namely pro vitamin A activity, antioxidant activity, protection against the risk of ultraviolet light, regulation of immune function, regulation and cell proliferation[5]. Red fruit juice testing against anticancer effects has been performed on uterine cancer cells, T47D breast cancer cells and colon cancer cells CC531. Impact on uterine cancer cells and colon cancer cells CC531 greater than in breast cancer cells[5]. Red fruit oil contains useful active compounds. However, this is less supported by the dosage form of red fruit oil not readily absorbed in the digestive tract because it is difficult to dissolve in the gastrointestinal tract[5].

The technology of pharmaceutical preparation and drug delivery systems in the process of discovering new pharmaceutical drugs to the public with the advantage of being able to penetrate intercellular spaces only permeable by the size of colloidal particles[6]. Nanoparticles are the latest drug delivery systems which can increase the rate of delivery of drugs to receptors[7]. In the development of pharmaceutical technology-based drug delivery systems, a provision is required that enhances the ability of active compounds to penetrate, one with the Self Nanoemulsifying Drug Delivery System (SNEDDS)[8].

Some of the potential advantages of SNEDDS include having the ability to present the drug in the form of dissolved in the lumen of the gastrointestinal tract (GI), thus providing a more extensive interface area for drug absorption[9]. SNEDDS is an isotropic mixture between oils, surfactants, and co-surfactants which can form spontaneous nanoemulsions when in contact with stomach fluids[10, 11]. The advantage of nanoemulsion in water is the ability to carry hydrophobic drugs in the oil so that they can be emulsified in water and ultimately increase the solubility of the drug while in the body[12]. Surfactants capable of contributing to solubilization and increase solubility of insoluble or slightly soluble material in the dispersion medium. It plays a role to reduce surface tension and increase the solubility rate of the drug wherein sugar ester is a nonionic surfactant comprising sucrose as hydrophilic and fatty acid groups as lipophilic groups that are tasteless, odorless, non-toxic and may be used as excipients in drugs and cosmetics because they do not irritate the eyes and skin[13].

SNEDDS as a delivery system increases the bioavailability

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Table 1: Formulation SNEDDS of Red Fruit Oil.

Formulation	Sucrose monoester + Tween (%)	Propylene Glycol (%)	Red Fruit Oil (%)
I	62.5	17.5	10

Table 2: Particle size, zeta potential, and polydispersity Index of optimized SNEDDS formulation during storage (n=3).

Formulation	Particle size (nm)	Zeta Potential (mV)	Polydispersity Index
1	193.1 ± 1,68	-43.26 ± 0.11	0,50 ± 0.01

of lipophilic drugs so that oral bioavailability in water-insoluble drugs can be enhanced by formulating with lipids[14]. However, research conducted only limited to the development of formulations and the absence of cancer cell tests in the form of a validated dosage. The purpose of this study is to preparation and characterization of MCF-7 breast cancer cell test in Self-Nano Emulsifying Drug Delivery System (SNEDDS) loading red fruits.

MATERIALS AND METHOD

Materials

Red fruit oil was a gift from Made Mulya Asih Ltd. Indonesia, tween 20 and propylene glycol were purchase from Brataco Indonesia Ltd., sucrose monoester palmitate (P-1670 Ryoto® Japan), Culture Media M199, DMSO 1%, MTT 0.5 % and all ingredients used are available at Pharmaceutical Technology Laboratory at Islamic University of Indonesia.

Preparation of SNEDDS

This study began with a working sequence of manufacturing SNEDDS using sucrose monoester palmitate (SME), propylene glycol (PG), tween 20 and red fruit oil. The solubility of red fruit oil in different oils, surfactants, and co-surfactants are 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 carried out by mixing the red fruit formulation into the surfactant and the cosurfactant. Then the particle size determination, zeta potential determination, and polydispersity index were characterized. The formulation can be seen in table 1.

Preparation of Cell Cancer

To perform the test sample carried out a cancer cells MCF-7 cell, after enough then the cells at harvest, and then carried out a test of cancer cells with MTT ASSAY. The results of the calculation of the viability of cells obtained from each concentration, then proceed with the test correlation equation of linear regression to determine and specify the value of IC_{50}. The linear regression equation obtains IC50 values ($y = bx + a$) of the graph between the log concentration versus % living cells where the value of r is said to be linear if is higher than table then put the value of $y = 50$ linear regression equation on and searched x, then determined the concentration of antilog retrieved IC_{50}.

RESULTS AND DISCUSSIONS

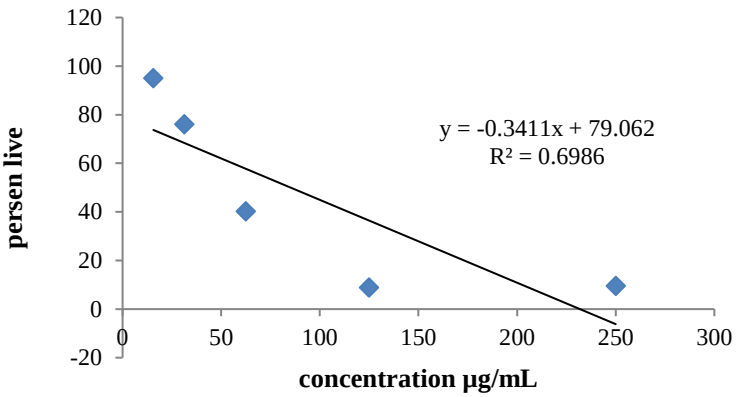
Evaluation of SNEDDS

Determination of particle size, zeta potential, and Polydispersity Index was performed using Particle Size Analysis (PSA). The results are presented in table 2. Self-Nano Emulsifying Drug Delivery System (SNEDDS) from red fruit oil with the good particle size is 193.1 ± 1.68 nm, with ratio red fruit oil: surfactant: co-surfactant (10: 62.5: 17.5). In this formulation zeta potential value showed -43.2 ± 0.11, and 0.50 ± 0.01 of polydispersity index (PDI).

Zeta Potential is a scientific term for potential electro kinetics in a colloidal system, and zeta potential 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 the nanoparticles' surface will prevent the aggregation of the nanoparticles due to the strong repulsive force between particles. The zeta potential value was -43.26 ± 0.11 mV. As a rule of thumb, potential zeta values ± 30 mV will provide good stability, and ± 60 mV have excellent stability[16]. It can be explained that 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 SNEDDS 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[17].

The particle size value was 193.6 ± 1,68 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 increase the absorption of red fruit oil in SNEDDS dosage forms. It can be explained that the co-surfactant with small molecules can improve the emulsification function of surfactant by penetrating the surfactant film on the oil-water interface. Therefore, this condition will decrease interfacial tension and enhanced spontaneous emulsification process. The required free energy to create small globule size in a self-emulsifying system is deficient, causing spontaneous formation of oil nanoemulsion in water[18].

The polydispersity index (PDI) 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 particle 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 is 0.50 ± 0.01. The PDI value of this formula falls



Y	50
b	-0.3411
a	79.062
IC50	85.20 µg/mL

Table 3: Study of cell MCF-7 with SNEDDS red fruit oil.

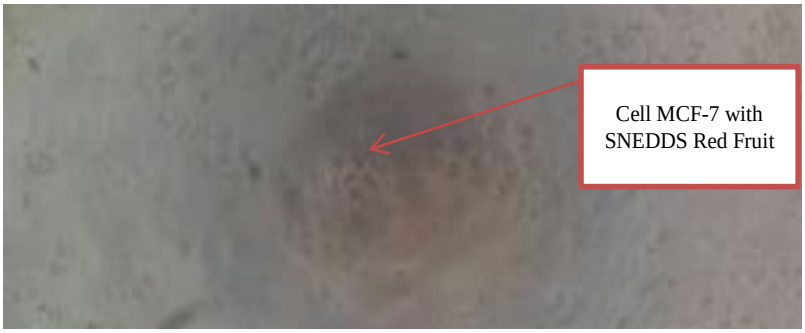


Figure 1: Cell Cancer MCF-7 with SNEDDS Red Fruit Oil.

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[18]. Clarity measured in per cent transmission is one of the controls for dispersion formation from SNEDDS. Visual observation of clarity is a qualitative parameter of dispersion spontaneity. The Transmittance value which is close to 100% indicates that SNEDDS produces a clear and transparent dispersion with droplet sizes estimated to reach nanometers[19].

Study of cell MCF-7 with SNEDDS red fruit oil

The study of cell MCF-7 with SNEDDS red fruit oil as shown in table 3 and figure 1. The final result of the cytotoxic test may provide information on the maximum drug concentrations that still allow cells to survive[20]. Formazan crystal formation is purple and needle-shaped after MTT administration. More formazan crystals are formed by many cells which are still alive because MTT will only experiment with various forms of crystals[21]. Two conventional methods used for cytotoxic tests are straightforward counting methods, such as direct calculations using trypan blue and indirect counting methods, such as the MTT assay method. A cytotoxic test is used to determine the IC_{50} value parameter. The value of IC_{50} shows the concentration value which results in cell proliferation resistance of 50% and shows the cytotoxic effect of a compound on the cell. The higher the amount of IC_{50} the compound is less toxic and characterization of cell cancer MCF- 7 shows IC_{50} 85.20 µg/mL. The proliferation of SNEDDS red fruit against anti-growth arresting MCF-7 cell line, this case demonstrates that it may exert its proliferative effect by reducing DNA synthesis and apoptosis-inducing cell cycle stages[22].

CONCLUSIONS

The formulation of red fruit SNEDDS showed a good of particle size (193.1 ± 1.68), zeta potential (-43.26 ± 0.11 mV), and polydispersity Index (0.50 ± 0.01) with a ratio of oil: surfactant: co-surfactant of 10: 62.5: 17.5. The characterization of cell cancer MCF- 7 showed 85.20 µg/mL of IC_{50}. This formulation has cytotoxic activity against MCF-7 breast cancer cells.

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