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Effect of High Pressure Homogenizer on the Formation of Zingiber Officinale- Loaded Nanostructured Lipid Carrier

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Abstract – *Nowadays, nanostructured lipid carrier has been employed in pharmaceutics, nutraceuticals and biomedical formulations also other purposes. The aim of this study was to estimates the effect of high pressure homogenizer on the properties of zingiber officinale loaded nanostructured lipid carrier especially on size of particle and polydispersity index. Experiments were constructed using high pressure homogenizer by applying certain homogenizing pressure and cycle. The independent variables were homogenization pressure (0–2000 bar) and cycle (1-9) and the analysed responses were particles size and polydispersity index. The increase in the homogenization pressure up to 1300 bar and six cycle decreased the emulsion droplet size. However, the use of pressures above that pressure and cycle resulted in the formation of droplets with larger size.*

Keywords: Nanostructured lipid carrier, Zingiber officinale, High pressure homogenizer, Particle size

1.0 INTRODUCTION

Zingiber officinale (ZO) Roscoe or also known as ginger, ginger root or garden ginger is a medicinal plant in the family Zingiberaceae that has been widely used in China, India, and Jamaica whose rhizome, ginger root or simply ginger, is used as a spice or a folk medicine. It originated in Malaysia and India. Ginger plant gets about 1.2 m tall with leaves about 1.9 cm wide and 17.8 cm long. Ginger has been used for thounsands of years for relief from arthritis, rheumatism, sprains, muscular aches, pains, sore throats, cramps, constipation, indigestion, vomiting, hypertension, dementia, fever, infectious diseases and helminthiasis [1]. Ginger is very rich in minerals and chemical constituents such as gingerols, shogaols, 3-dihydroshogaols, paradols, dihydroparadols, acetyl derivatives of gingerols, gingerdiols, mono- and di-acetyl derivatives of gingerdiols, 1-dehydrogingerdiones, diarylheptanoids, and methyl ether derivatives of some of these compounds and [6]-gingerol itself,is the main bioactive constituent [1]. Recently, ginger has been the subject of various studies, notably in relation to its possible of anti-inflammantory, anti-diabetic, anticancer, antioxidant, antimicrobial, antifungal, antibacterial, antiviral, immuno-modulatory, anti-tumorigenic, anti-apoptotic, anti-hyperglycemic, anti-lipidemic and anti-emetic, reduce muscle pain, anti-analgesic, anti-hypoglycaemic, preventing gastrointestinal disorders, pneumonia, rheumatism and musculoskeletal disorders , antithrombotic, antimutagenic, and antidiarrhoeal properties [2-18].

Nanostructured lipid carrier (NLC) is one of the carrier agents in drug delivery system which developed for encapsulation of bioactive compounds in biological, pharmaceutical, medical, nutritional and cosmeceutical research. NLC is developed to overcome some potential limitations associated with solid lipid nanoparticles. Compared to it, NLC show a higher loading capacity for a number of active compounds, a lower water content of the particle suspension and avoid and minimize potential expulsion of active compounds during storage. In the NLC very different lipids were blended to form the matrix, which means solid lipids and liquid lipids. Many different techniques for the production of lipid nanoparticles have been described in the literature. These methods are high pressure homogenization, microemulsion technique, emulsification-solvent evaporation, emulsification-solvent diffusion method, solvent injection method, multiple emulsion technique, ultrasonication, and membrane contractor technique [19].

High Pressure Homogenizer (HPH) is one of the technological process aiming at the reduction in size and uniformity of fat globules, thus their even dispersion in emulsion and an increase in emulsion stability. HPH are widely used in many industries including pharmaceuticals and nutraceuticals industry. It has many advantages compared to others method because it properties that are easy to scale up, avoidance of organic solvents and short production time. Therefore, this study analyze the effect of HPH on properties of the production of *zingiber officinale* encapsulated nanostructured lipid carrier (ZO-NLC), particularly on its size.

2.0 METHODOLOGY

2.1 Materials

Polyoxyethylene sorbitan monooleate (Tween® 80), Sephadex® G-50, and L-α-Phosphatidylcholine (soy lecithin) were purchased from Sigma-Aldrich (Selangor, Malaysia). Chinese ginger oil (zingiber officinale oil) was obtained from Wellness Original Ingredient; (Selangor, Malaysia).Virgin coconut oil was supplied by Institute of Bioproduct Development (Universiti Teknologi Malaysia, Malaysia). All other chemicals and reagents used in the study such as glyceryl monostearate and microkil were of analytical grade. Distilled water was used throughout the experiment.

2.2 Preparation of Zingiber Officinale Oil-loaded NLC

Zingiber Officinale oil incorporated in nanostructured lipid carrier (ZO-NLC) was prepared according to the method reported by Rosli et al. (2015) with some modifications [20]. Tween® 80 was chosen as the surfactant. Initially, a certain amount of active compound (ZO oil) was dissolved in a mixture of liquid lipid (virgin coconut oil) and melted solid lipid (glycerol monostearate). The lipid melt containing active compound is then dispersed in a hot surfactant solution (temperature 5-10°C above the melting point of solid lipid) by high speed stirring (IKA T-25 ULTRA-TURRAX® Stirring, Selangor, Malaysia) at 17 000 rpm for five minutes. The obtained emulsion is then passed through high pressure homogenizer (IKA High Pressure Homogenizer HPH 2000/04, Selangor, Malaysia) following required cycles (1-9 cycle) and pressure (300-2000 bar), to produce ZO-NLC. The minimum volume of the samples processed is 100 mL. All homogenizations are carried out above the transition temperature of the NLC.

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Subsequently, the NLC dispersion was cooled in ice water bath to room temperature (25±1°C) and stored at 4°C.

2.3 Particle Size and Polydispersity Index Analysis

The particle size and polydispersity index (PI) of ZO-NLC was measured through photon correlation spectroscopy (PCS) (Dynamic Light Scattering, DLS, Zetasizer Nano NS, Malvern Instruments, Malvern, UK) at 25^{0}C using disposable plain folded capillary. Each measurement was performed in triplicate and the refractive indices of nanoparticles and water were set at 1.54 and 1.33, respectively. To avoid multiple scattering effects in the formulation, the ZO-NLC was suitably diluted (1:10) and the vortexed to measure mean particle size and polydispersity index.

3.0 RESULTS AND DISCUSSION

The results of the effect of homogenization pressure on particle size (PS) and polydispersity index (PI) of ZO-NLC presented in Figure 1.The homogenization pressure represents the level of energy applied to the liquid as it goes through the valve. A portion of this energy subdivides the droplet, but most of it is converted into heat after homogenization is completed. It is estimated that less than 0.1% of the energy is used for emulsification. This is based on the work needed to create the new, total surface area in the final emulsion. This is not to say that the energy is wasted, because the subdivision of the droplets is a complex process, and homogenization requires this total energy level to initiate the action. As expected, the homogenization processing reduced the particle size, as it increased [21-22]. Moreover, as can be seen in Fig. 1 and 2, not only was the particle size affected by the HPH but also the polydispersity index. Polydispersity Index indicated the distribution size in the Z0-NLC and the accepted or the best result was (<0, 3). The ZO-NLC operated at 0 bar act as control sample showed a particle diameters ranging between 1000 to 2000 nm. When the ZO-NLC was processed at 300- 2000 bar, a smaller size was observed, with particles ranging between 200 to 400 nm. When the homogenization pressure varied from 300 to 1300 bar the oil droplet size decreased with the increase in the homogenization pressure, probably due to the higher amount of energy provided to break the emulsion droplets. However, the use of pressures above 1500 bar resulted in the formation of droplets with larger size. This is due to newly disrupted droplets are thermodynamically unstable due to the Brownian motions and high intensity turbulence on the equipment and increasing the probability of collision and coalescence of freshly formed droplets to form bigger droplets [21]. As a result, final emulsions would have a bigger droplet size.

Many applications require a very uniform droplet-size distribution in the generated emulsion, either for control of creaming rate or for some physical action or characteristic required of the emulsion. This can be accomplished in the homogenizer by passing the product through the valve more than once. Because the homogenization process is random in nature, the size distribution follows a log-normal distribution curve. This means that the curve is asymmetrical and contains a "tail" representing oversized particles. With one pass through the homogenizer, there is a certain probability that not all particles are subjected to the same intense energy of homogenization; therefore, a portion of the particles passes through without being as reduced in size as others. Another pass through the homogenizing valve increases the probability of these large particles being reduced. Therefore, multipassing through the valve narrows the particle-size distribution can help in reducing size of particles.

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Figure 2 below shows the effect of HPH cycle on ZO-NLC properties. As shown as figure below, the particles size and polydispersity index of ZO-NLC are significantly reduce from cycle one to 6 but rapidly increasing after cycle six. It happened because after six cycles, the ZO droplet start to break the NLC wall due to the unsuitable cycle was applied.

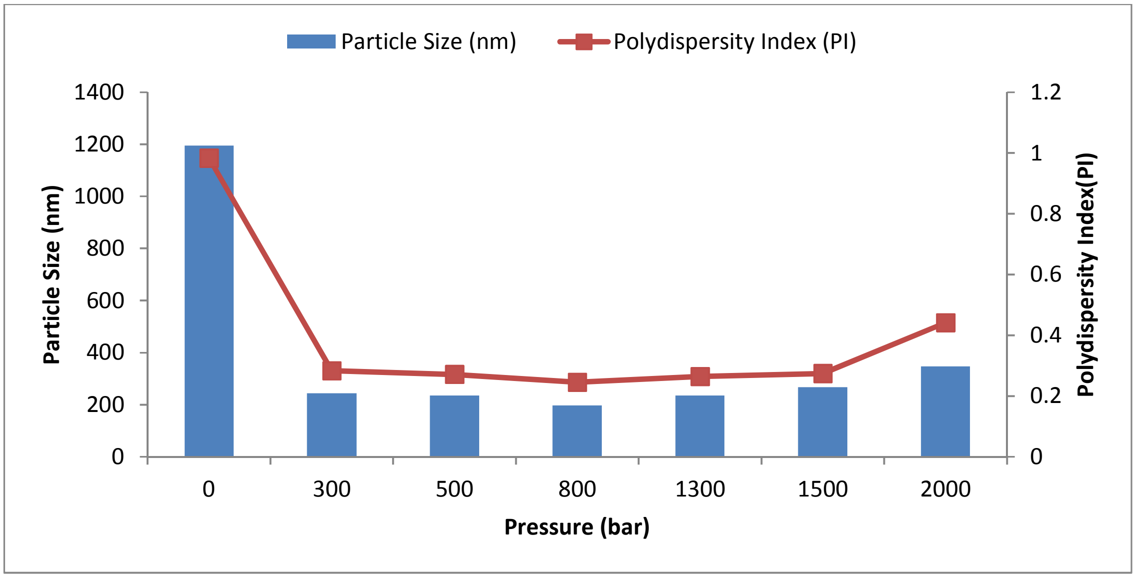

Figure 1: Effect of HPH pressure on ZO-NLC properties

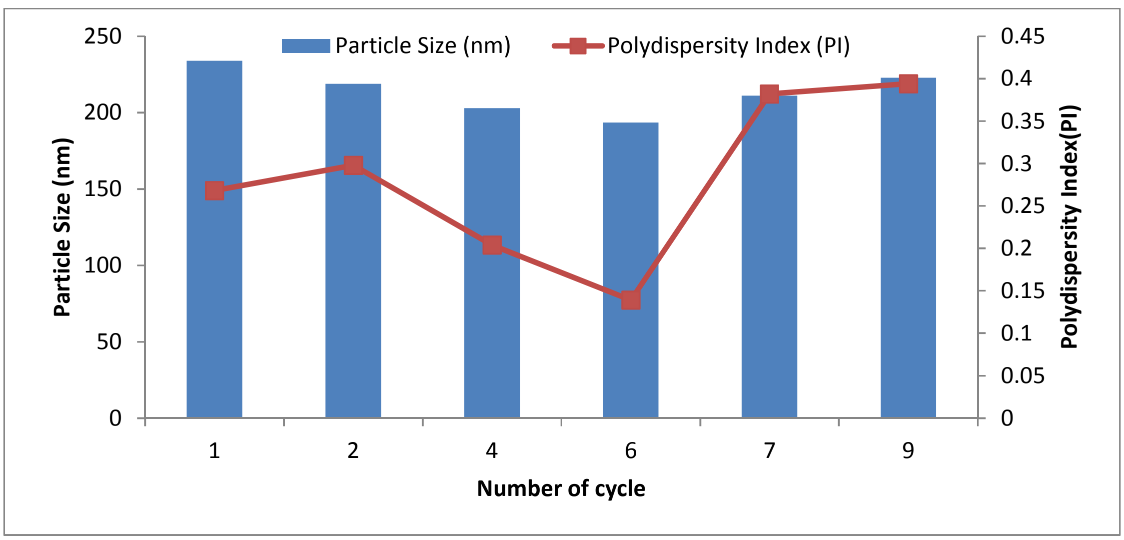

Figure 2: Effect of HPH cycle on ZO-NLC properties

4.0 CONCLUSSION

The present work evaluated the effect of high pressure homogenizer on the particle size and polydispersity index properties of ZO-NLC. HPH reduced the particle size and polydispersity index as the pressure and cycle were adjusted up to certain limit. The changes observed may be mainly caused by the high pressure and shear applied during homogenization while increase

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in the number of cycle was not high enough to cause such changes. It can concluded that, HPH was an efficient technology and method for reducing the droplet size of emulsion.

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