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Research Article

USAGE OF SUGAR ESTER IN THE PREPARATION OF AVOCADO OIL NANOEMULSION

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ABSTRACT

Objectives: Due to the high dynamics of pharmaceutical products markets, developments of new products using latest innovative technology are becoming a norm of many pharmaceutical companies. Nanoscale materials such as nanoemulsion (NE) offer advantages such as the controllable droplet size, long-term stability, and power solubilization ability. It is beneficial in various delivery systems either for transdermal, ocular, nasal, vaginal, and parenteral drug delivery. The objective of the study was to prepare avocado oil NE using different surfactants to find the most suitable nanosized droplets, as avocado oil offers a variety of purported nutritional and medicinal benefits.

Methods: Sucrose esters, glycerol, and avocado oil with different ratio were used to produce pre-NE by phase inversion technique then pre-NE were self-emulsified with water to produce NE. The influence of the sucrose esters surfactants on the NE formulations were determined using three different types of sucrose esters surfactant (laureate, oleate, and palmitate). Stability study was conducted for NE at different temperatures (4°C, 25°C, and 40°C) for 6 months.

Results: The NE contained sucrose laureate produced best nanosized formulations compared to other oleate and palmitate, with optimum droplet size 106 ± 1.70 nm, size distribution 0.156 ± 0.01, and zeta potential −30.4 ± 0.70. The NE formulations were very stable at 4°C compared to 25°C and 40°C while at 25°C NE showed moderate stability, but it was unstable at 40°C.

Conclusion: Sucrose laureate was able to produce NE with phase inversion and self-emulsification techniques and the ideal storage condition for NE is 4°C.

Keywords: Avocado oil, Nanoemulsions, Self-nanoemulsification, Phase inversion technique, Sucrose ester, Stability.

INTRODUCTION

Emulsions are one of the main pharmaceutical dosage forms in delivering active ingredients to the target area. It is being applied in several of industries, such as food applications [1,2] and pharmaceutical cosmetics [3,4]. Nanoemulsions (NE) are designed and named according to their droplet size, which is in nanometers ranging between 20 nm and 200 nm [5-7]. NE find applications in many pharmaceutical fields such as target drug delivery, controlled drug delivery, and have high solubilization capacity, which allows incorporation of large amount of drug when compared to other conventional topical preparation such as emulsions, gels, creams, and ointments [8]. In addition, they are used as topical and transdermal drug delivery because they modified the affinity of the drug to the internal phase in NE easily which leads to higher permeation rate of drug [9,10]. Finally, the interaction of NE to stratum corneum can improve transdermal drug permeation by changing the structural organization of its lipid layers [11]. Avocado has many therapeutic benefits due to the presence of high amount of oleic monounsaturated fatty acids and high amount of proteins [12-14]. It also gives health benefits to the cardiovascular system because it promotes the accumulation of high-density lipoprotein cholesterol [15,16], useful as anti-inflammatory agent [17]. Antioxidant [18,19] and in cancer prevention [19]. In addition to that, it is useful as skin care product due to the presence of mineral content and vitamin, as well as other nutrients in it [20]. The present work is aimed to study the influence of different sucrose ester surfactants on the production of avocado oil NE. It also helps in selecting the best sucrose ester surfactant which able to produce NE by the use of two technique heat inversion and self-emulsification techniques.

METHODS

Avocado oil (Sigma-Aldich, South Africa), sucrose esters (laureate, oleate, and palmitate) (Juhalim, Malaysia), and glycerol (HMBG Chemicals, Malaysia) were used in the preparation of NE by heat inversion and self-emulsification techniques. Three pseudo-ternary phase diagram was constructed using mixtures of avocado oil, sucrose esters, and glycerol to prepare the pre-NE. The three mixtures were, mixture 1 consists of oil, laureate, and glycerol; 2 consists of oil, palmitate, and glycerol; and 3 consists oil, oleate, and glycerol. Each formulation weighing 10 g were prepared first by heating glycerol to 75°C using hot plate (Carolina Biological Supply, USA) after that the surfactant was added to the hot glycerol and mixed using glass rod until it was dissolved the temperature was maintained to about 75±5°C, then the oil was added to the surfactant mixture at the same temperature and mixed until the mixture cool down to the room temperature. Then pre-NE were diluted with distilled water to 100 ml at room temperature under gentle agitation to produce NE by self-nanoemulsification technique. The NE formulations were tested for their droplets size and size distribution using Malvern Mastersizer 2000, also zeta potential (ZP) was tested using Malvern Zetasizer in triplicate. To observe the size and distribution of the droplets, a 250 µl sample was examined using a Mastersizer. Finally, NE optimum formulation was stored at different temperatures (4°C, 25°C and 40°C) for 6 months, NE samples were tested initially, after 3 months and at 6 months of storage.

RESULTS AND DISCUSSION

The ternary phase diagram constructed and presented in Fig. 1, was used to aid in finding the concentration range of NE components. It can be seen from the ternary phase diagrams, different areas that correspond to different emulsions, such as transparent NE, macroemulsion, and coarse

emulsion. Sucrose laureate was able to produce NE region compared to palmitate and oleate. This is due to laureate high emulsification properties compared to sucrose palmitate and oleate, which may be due to its good miscibility properties [21]. Same findings were stated by Szuts and Szabo-Revesz [21] who mentioned that sucrose laureate was good in preparing solid dispersion due to its good has miscibility properties in water compared to sucrose palmitate and stearate. Furthermore, found that NE that used high hydrophilic-lipophilic balance (HLB) value like sucrose laureate as surfactant has better emulsification properties [22,23].

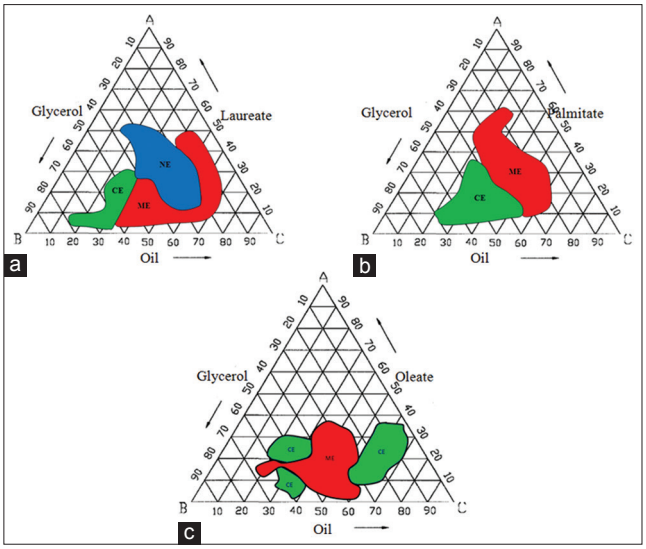

Fig. 1: Ternary phase diagrams, for avocado oil, sucrose esters (a) Laureate, (b) palmitate, (c) oleate and glycerin

Table 1 shows the selected formulations from the ternary phase diagram, which has droplets size below 200 nm. Among them Formulation A consisted of 16% w/w sucrose laureate, 24% w/w glycerol, and 60% w/w oil has the lowest amount of surfactant; and smallest droplets size 106±1.70 nm with size, distribution 0.156±0.01, and the ZP was −30.4±0.70 mV indicating high stability [24,25].

The results obtained in Figs. 2 and 3, showed the stability effect of different temperatures on NE formulations, in order to find the best storage condition of NE. Statistical results showed that there were no significant differences ($p>0.05$) in the droplet size and size distribution of NE formulations after 3 months storage at 4°C and 25°C. Droplet size and size distribution for Formulation A stored at 4°C were 109±2.6 nm and 0.158±0.03, Formulation B 165±5.50 nm and 0.226±0.03, Formulation C 167±4.10 nm and 0.248±0.03, and for Formulation D 147±2.60 nm and 0.198±0.02. The results of the formulations droplet size and size distribution at 25°C were as follow, Formulation A 144±2.8 nm and 0.179±0.03, Formulation B 185±5.50 nm and 0.256±0.03, Formulation C 183±4.10 nm and 0.273±0.04, and for Formulation D 180±2.60 nm and 0.225±0.01. Similar results were stated by Affandi *et al*. who stated that astaxanthin NE stored at 5 and 25°C for 3 months showed no significant changes [26].

While after 6 months, the formulations stored at 25°C showed significant difference in their droplets size and size distribution, Formulation A 158±6.6 nm and 0.189±0.02, Formulation B 228±5.20 nm and 0.439±0.03, Formulation C 255±3.80 nm and 0.442±0.04, and Formulation D 283±4.70 nm and 0.376±0.04. However, there were no difference in the droplet size and size distribution at 4°C, as the results were as follow, Formulation A 112±2.8 nm and 0.167±0.02, Formulation B 185±5.50 nm and 0.286±0.08, Formulation C 207±4.10 nm and 0.263±0.04, and Formulation D 192±2.60 nm and 0.251±0.02.

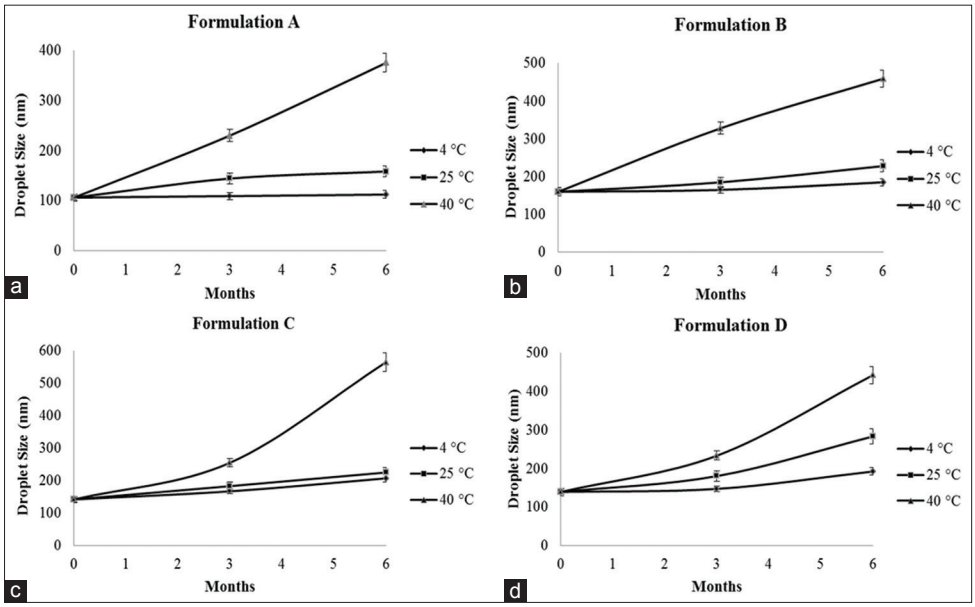

Fig. 2: Stability effect on droplet size of nanoemulsion formulations: (a) Laureate 16%, glycerol 24% and oil 60%, (b) laureate 40%, glycerol 25%, and oil 35%, (c) laureate 30%, glycerol 20%, and oil 50%, (d) laureate 20%, glycerol 30%, and oil 50%

Table 1: Droplets size, size distribution, and ZP for the NE

Formulation	Sucrose laureate (%)	Glycerol (%)	Avocado oil (%)	Droplet size (nm)	Size distribution	ZP (mV)
A	16	24	60	106±1.70	0.156±0.01	−30.4±0.70
B	40	25	35	160±2.10	0.220±0.03	−25.9±0.70
C	30	20	50	142±1.50	0.223±0.04	−25.0±1.00
D	20	30	50	139±1.50	0.189±0.02	−26.8±0.60

Mean±SD (n=3). Each formulation was self-emulsified in distilled water to 100 ml, SD: Size distribution, ZP: Zeta potential, NE: Nanoemulsion

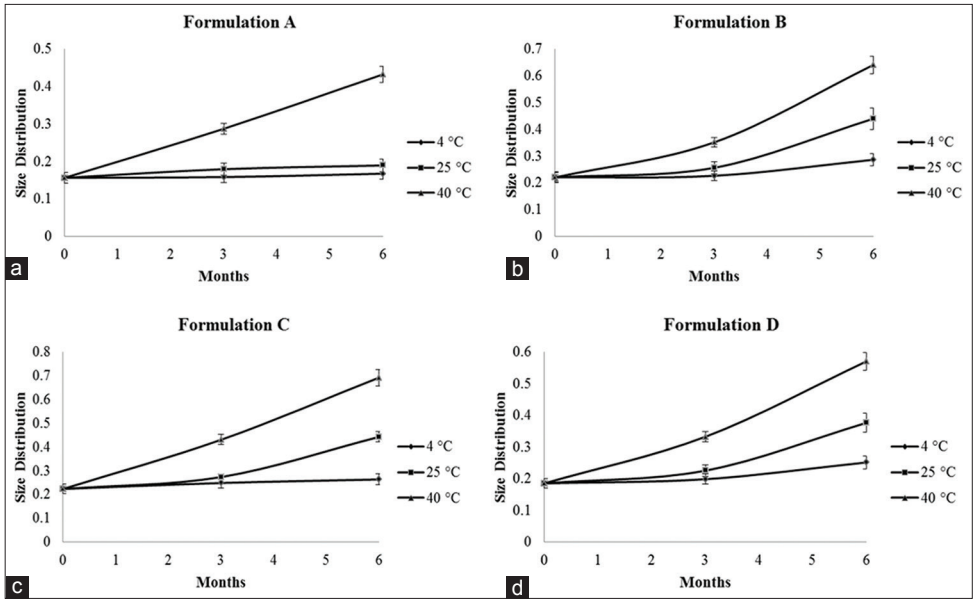

Fig. 3: Stability effect on size distribution of nanoemulsion formulations: (a) Laureate 16%, glycerol 24%, and oil 60%, (b) laureate 40%, glycerol 25%, and oil 35%, (c) laureate 30%, glycerol 20%, and oil 50%, (d) laureate 20%, glycerol 30%, and oil 50%

However, there was a significant difference on droplet size and size distribution for all of the formulations stored at 40°C after three and 6 months. There results after 3 months were as follow, Formulation A 230±6.6 nm and 0.287±0.02, Formulation B 328±5.20 nm and 0.351±0.02, Formulation C 255±3.80 nm and 0.430±0.04, and Formulation D 233±4.70 nm and 0.332±0.03. Furthermore, the results of those formulations after 6 months of storage were Formulation A 375±3.4 nm and 0.432±0.03, Formulation B 459±4.10 nm and 0.640±0.04, Formulation C 565±2.30 nm and 0.692±0.03, and Formulation D 443±3.20 nm and 0.570±0.02. Overall, from the results above the ideal storage temperature for these formulations is 4°C. This finding is with support by Sevcikova *et al*., who mentioned that the best stability condition of NE was observed at 4°C temperature [27].

CONCLUSION

In this work, avocado oil NE was prepared using two technique heat inversion and self-emulsification. The influences of sucrose ester and stability on NE were investigated. In general, sucrose laureate showed good emulsification properties due to its high HLB value, which make it able to produce NE when compared to palmitate and oleate. The optimum NE formulation produced consists of 60% oil, 16% laureate, and 24% glycerol. In addition, NE stability was most affected by storage temperature and showed high stability when stored at 4°C and moderate stability when stored at 25°C, but it was unstable at 40°C. Therefore, the best storage condition of NE when stored at 4°C.

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