

## 조성 상전이 방법으로 제조된 안정한 액상 파라핀-물 나노에멀전

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### Stable Liquid Paraffin-in-Water Nanoemulsions Prepared by Phase Inversion Composition Method

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**요약:** 물/Span 80-Tween 80/긴 사슬 파라핀 오일 계에서 PIC (조성 상전이) 방법을 이용하여 O/W 나노에멀전을 제조하였다. 제조 온도를 30 °C에서 80 °C로 상승시킴에 따라 제조된 나노에멀전의 입경은 120 nm에서 40 nm로 감소하여 나노에멀전을 형성하였다. 혼합 계면활성제의 HLB를 변화시킴에 따라 12.0 ~ 13.0 부근에서 가장 작은 입경을 형성하는 최적 HLB가 존재하였다. 나노에멀전의 점도는 액적의 부피 분율( $\phi$ )에 따라 현격하게 증가하였으나, 입경의 크기는 약간 증가하였다. 그리고,  $\phi \leq 0.3$  조건에서 나노에멀전의 크기 분포는 2개월 이상 일정하게 유지 되었다. 이러한 결과는 점성 파라핀 오일의 경우 30 °C에서는 PIC 방식으로 거의 분산할 수 없음을 보여주지만, 제조 온도가 증가할 경우 단 분산 나노에멀전의 제조가 가능하다는 것을 보여준다. 나노에멀전이 생성되면, Ostwald ripening에 대한 안정성은 연속 상에서 액상 파라핀 오일의 매우 낮은 용해도로 인해 안정하게 되며, 이는 화장품 응용에서 매우 중요하다.

**Abstract:** Oil-in-water nanoemulsions were prepared in the system of water/Span 80-Tween 80/long-chain paraffin oil via the PIC (phase inversion composition) method. With the increase of preparation temperature from 30 °C to 80 °C, the diameter of emulsion droplets decreased from 120 nm to 40 nm, proving the formation of nanoemulsions. By varying the HLB (hydrophilic lipophilic balance) of mixed surfactants, we found that there was an optimum HLB around 12.0 ~ 13.0 corresponding to the minimum droplet size. The viscosity of nanoemulsions clearly increased with droplet volume fraction,  $f$ , but the droplet size slightly increased. Significantly, at  $\phi \leq 0.3$ , the size distribution of nanoemulsions kept constant more than 2 months. These results proved that the viscous paraffin oil can hardly be dispersed by the PIC method at 30 °C, but the increase in preparation temperature makes it possible for producing monodisperse nanoemulsions. Once the nanoemulsion is produced, the stability against Ostwald ripening is outstanding due to the extremely low solubility of the liquid paraffin oil in the continuous phase. The highly stable nanoemulsions are of great importance in cosmetic applications.

**Keywords:** Liquid paraffin, Nanoemulsion, PIC, Ostwald ripening, Cosmetics

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## 1. Introduction

The potential benefits of cosmetic nanoemulsions include optical clarity, good stability to gravitational separation, flocculation and coalescence, and improved absorption and bioavailability of functional components[1]. A deeper understanding of the basic physiochemical properties of nanoemulsions would, therefore, provide key information to better guide formulation and application of nanoemulsion to cosmetics.

Nanoemulsions can be prepared by high or low energy emulsification methods[2-4]. High energy emulsification methods require large mechanical energy generated by high pressure homogenizers or ultrasound generators to produce fine droplets. In contrast, low energy emulsification methods can take advantage of the chemical energy stored in the ingredients and produce the nanoemulsions almost spontaneously, thus have great attraction both in theoretical study and practical application. The change in the spontaneous curvature of surfactants during the emulsifying process has been recognized to be a key factor for the formation of nanoemulsions, which can be achieved either by changing the temperature (phase inversion temperature, PIT method) or by changing the volume fraction of water or oil (phase inversion composition method, PIC method)[2-4]. Paraffin oil has been applied in many cosmetic products as a component of O/W emulsions, mostly as macroemulsions. The formation of paraffin oil emulsions with submicron droplets using the PIC method has occasionally been reported[4,5]. Sagitani et al. suggested that a proper HLB value of the surfactants was a key factor for the formation of emulsion with minimal droplets[5]. Dai et al. observed that the molecular structure of emulsifiers had a great effect on the droplet size of the final emulsions[6]. Fernandez et al. attained paraffin oil nanoemulsions with droplet sizes of 300 ~ 500 nm with surfactant-to-oil weight ratios of 0.364 and 0.5 at 80 °C[4].

In the present work, we obtained paraffin oil-in-water nanoemulsions at different emulsification temperatures using the PIC method. We optimize the droplet size of

nanoemulsions by varying the HLB of Tween 80 and Span 80.

## 2. Materials and Methods

### 2.1. Materials

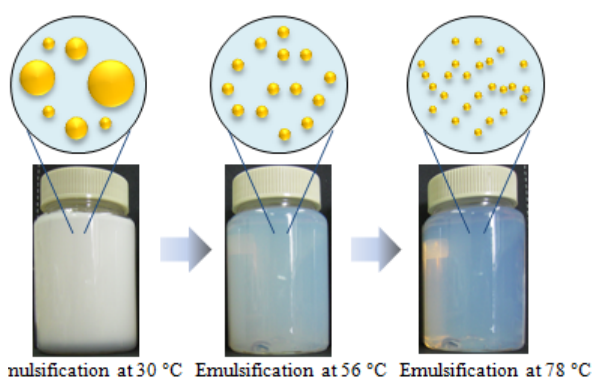
The liquid paraffin (Lily 70, cosmetic grade), Sorbitan monooleate (Span 80, cosmetic grade), and polyoxyethylene (20) sorbitan monooleate (Tween 80, cosmetic grade) were obtained from Kukdong Oil & Chem. Ltd, Ilshin wells Co. Ltd. and Croda Chem., respectively. The components of this paraffin oil are light mixtures of alkanes in the C15 to C40 range with specific gravity of 0.831 and viscosity of 11.0 ~ 13.5 cSt at 40 °C. All reagents were used as received without further purification. Water was deionized and Milli-Q filtered.

### 2.2. Preparation of nanoemulsions

Before emulsification, the surfactants (Span 80 and Tween 80) were dissolved into the oil phase under magnetic stirring. The surfactant-oil mixture and water were placed separately in a water bath at the desired temperature. Then the water phase was added dropwise to the oil solution. After the emulsification, the samples were cooled at room temperature (~ 25 °C). The influence of composition parameters, including the oil-to-surfactant weight ratio (O/S) and the droplet volume fraction ( $\phi$ ), was investigated systematically. Moreover, the formation of nanoemulsions depends not only on composition variations but also on preparation conditions[7,8]. Therefore, the experimental parameters were maintained constant at a stirring rate of 400 rpm and an addition rate of 2 mL/min.

### 2.3. Droplet size determination

Nanoemulsion droplet size and distribution were determined by dynamic light scattering (ELS-8000, Otsuka, Japan). A 200 mW green laser ( $\lambda = 532$  nm) with variable intensity was used, and measurements were carried out at room temperature with a scattering angle of 90 °. The droplet size was measured directly without dilution.



**Figure 1.** Schematic diagram and photograph of nanoemulsions prepared varying different emulsification temperature.

The average radius were calculated from the intensity autocorrelation data with the cumulant method. The time-intensity correlation functions were analyzed by the CONTIN method[9].

#### 2.4. Long-term stability test

The long term stability of nanoemulsions was assessed by measuring the change of droplet size with time of storage. The samples were kept sealed at room temperature.

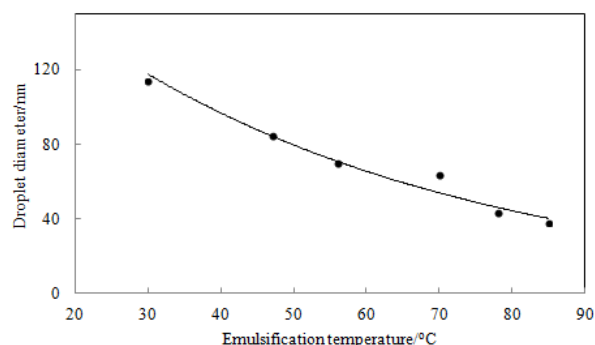
#### 2.5. Viscosity

The viscosity of nanoemulsions was measured by DV-E viscometer (RT, Brookfield, USA) using a #4 spindle and a rotational speed of 60 rpm at 25 °C.

### 3. Results

#### 3.1. Effect of emulsification temperatures at fixed composition

The schematic diagram and photograph of the nanoemulsions as a function of the preparation temperature is shown in Figure 1. The turbidity of emulsions is decreased as increasing the emulsification temperature. In Figure 2, droplet diameter decreases from 113.9 to 43.2 nm with the increase of emulsification temperature at a constant composition (O/S = 1 : 1,  $\phi = 0.1$ ). The droplet



**Figure 2.** The effect of emulsification temperature on emulsion droplet diameter for samples with O/S = 1 : 1 and  $\phi = 0.1$ .

size decreases with the increase of emulsification temperature from 30 to 80 °C and remain unchanged with a further increase in the temperature. L. Yu et al. reported that nanoemulsions cannot be obtained at low temperature due to the relatively high interfacial tension and the high viscous resistance of the oil phase. With the increase of preparation temperature, the amount of surfactant molecules adsorbed at the O/W interface increases gradually. At elevated temperatures ( $\geq 70$  °C), the surfactant adsorption reaches saturation[10].

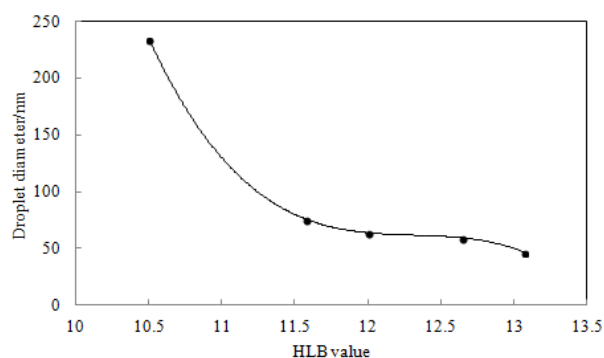
#### 3.2. Effect of HLB on emulsification at elevated temperature

As stated above, the droplet size distributions remain unchanged when the emulsions are prepared at 70, 78, and 85 °C. The temperature of preparation is fixed at 70 °C for further investigations. In this section, we examined the influence of HLB value and O/S on nanoemulsion formation. When the emulsion is stabilized by a mixture of nonionic surfactants, the mixed HLB value is considered to be the algebraic average of the HLB value of the individual surfactants.

In other words, the variation in the mixed HLB values was calculated according to the relationship

$$HLB_{\text{mix}} = HLB_A \times A\% + HLB_B \times B\% \quad (1)$$

where  $HLB_{\text{mix}}$  is the HLB value of the mixed surfac-

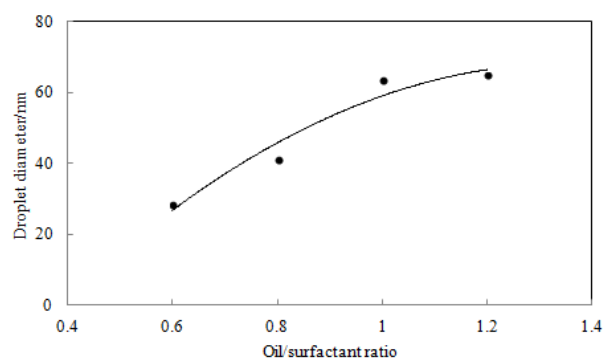


**Figure 3.** Droplet diameter as a function of the HLB value for samples with O/S = 1 : 1,  $\phi = 0.1$  and preparation Temp. = 75 °C.

tants,  $HLB_{A/B}$  is the HLB value of surfactant A or B, and A% and B% are the weight percentages of A and B, respectively. All the HLB values used are obtained at 25 °C. The  $HLB_{mix}$  has little effect on the size distributions of nanoemulsions obtained by the PIT method[11]. In contrast, the droplet diameter prepared by the PIC method depends on both the surfactant mixing ratio and the preparation temperature[12,13]. Figure 3 shows the influence of HLB value on emulsion droplet size. Corresponding to the minimum droplet size, there is an optimum HLB region around 12 to 13.

The droplet diameter of samples with HLB 10.5 and 13.1 shows 233.7 and 46.5 nm, respectively. However, we obtained macroemulsions below the HLB of 10.5 and above 13.1. These macroemulsions were unstable and show creaming patterns within several days.

We examined the influence of O/S ratio on emulsion diameter of nanoemulsions, as presented in Figure 4. The droplet diameter increases from 28 to 67 nm as the O/S increases from 0.6 to 1.4. This variation tendency agrees with those reported earlier by the PIC method prepared at 25 °C[14]. Studies on nanoemulsion preparation by low energy methods have shown that the key to nanoemulsion formation could be attributed to the phase transitions occurred during the emulsification process[15]. The droplet size is governed by the surfactant phase structure (bicontinuous microemulsion or liquid crystal phase) at the inversion point induced by either temperature or composition[16]. As the ratio O/S above 1.4, we obtained



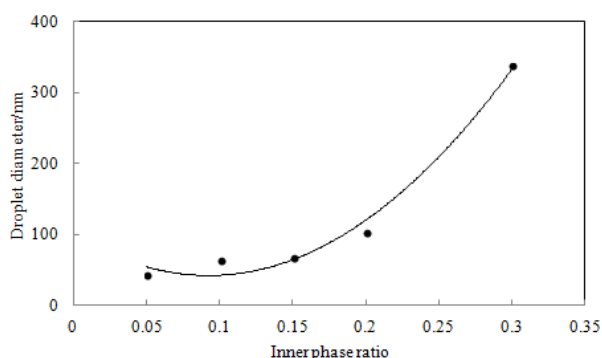
**Figure 4.** Droplet diameter as a function of the oil/surfactant weight ratio at HLB = 12.0.

macroemulsion which was unstable against creaming.

### 3.3. Formation of nanoemulsion by varying inner phase volume

In high energy methods, monodisperse nanoemulsions can be formed over a wide range of droplet volume fraction ( $0 < \phi \leq 0.3$ ) by the combination of high pressure homogenization and repeated ultracentrifugal fractionation at 18,000 rpm for 3 h[17]. The size distribution of these emulsions has not changed over months. However, using low energy methods, most nanoemulsions are prepared at relatively low volume fractions of the dispersed phase ( $0 < \phi \leq 0.3$ )[18]. The effect of  $\phi$  on the droplet size distribution has been studied less frequently because of the disadvantage on storage stability especially when the droplets are concentrated.

In our system, the droplet volume fraction, given by the oil volume fraction plus the surfactant volume fraction, was varied from 0.05 to 0.5 (Figure 5). The droplet diameter remains less than 350 nm when O/S is fixed at 1 : 1. The droplet size increases gradually as the volume fraction increases. However, in case of volume fraction 0.4 and 0.5, we cannot measure the droplet size. Generally, the droplet size is mainly governed by the structure of the bicontinuous phase during the phase inversion. Excess water acts only as a dilution medium. This is in agreement with the literature data showing that for emulsions produced by the PIT method[19]. This results does not agree with D. Morales and L. Yu[10,19].



**Figure 5.** Droplet diameter of emulsions with O/S = 1 : 1 as a function of  $\phi$ .

As the volume fraction increases from 0.05 to 0.4, the viscosity of nanoemulsions gradually increases. The viscosity of 0.4 ( $\phi$ ) is measured 60 cP by a #4 spindle and a rotational speed of 60 rpm using DV-E viscometer. However, the viscosity of a volume fraction of 0.5 increases dramatically and translucent gel is observed. It is thought to be a phenomenon caused by liquid lamellar phase formation rather than inner phase interaction.

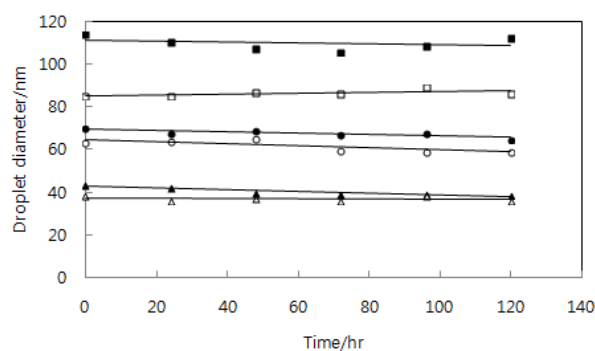
### 3.4. High Stability

Ostwald ripening is usually considered to be the major destabilization mechanism of nanoemulsions. It arises from the fact that oil solubility increases with decreasing droplet size. Large droplets grow at the expense of small ones in polydisperse emulsions due to molecular diffusion of the oil through the continuous phase. The rate of Ostwald ripening,  $\omega$  can be obtained by LSW (Lifshitz – Slezov – Wagner) theory[20]

$$\omega = dr^3/dt = 8\gamma C_{\infty} V_m D / 9RT \quad (2)$$

where  $r$  is the average droplet radius,  $t$  is the storage time,  $C_{\infty}$  is the bulk phase solubility,  $\gamma$  is the interfacial tension,  $V_m$  is the molar volume of the oil,  $D$  is the diffusion coefficient of the oil phase in the continuous phase,  $R$  is the gas constant, and  $T$  is the absolute temperature. Equation 2 predicts a linear relationship between the cube of the radius and time.

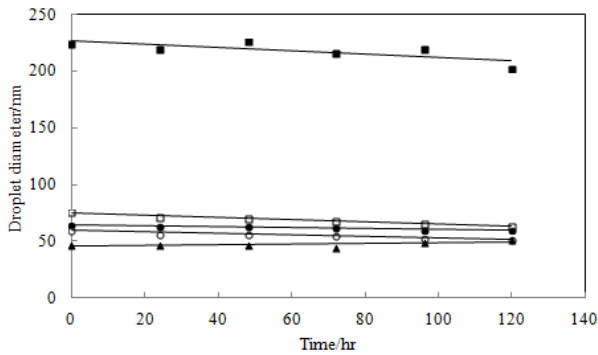
The main limitation for developing nanoemulsion appli-



**Figure 6.** Droplet diameter as a function of time for samples prepared at different emulsification temperatures of 30 °C (■), 47 °C (□), 56 °C (●), 70 °C (○), 78 °C (▲), and 85 °C (△) and stored at 25 °C (O/S = 1 : 1 and  $\phi = 0.1$ ).

cations is the relatively low stability. When the emulsification was produced by high energy methods, the stability of nanoemulsions could be improved by increasing the oil viscosity, corresponding to the decrease in  $C_{\infty}$ . The size distributions of these nanoemulsions have not changed over months[21]. But the disadvantages of these methods are the high energy cost and viscous heating[22]. For instance, the high-pressure homogenizers generally work in the pressure range between 50 and 100 MPa[23]. When nanoemulsions were prepared using low energy methods, the effect of carbon number of various n-alkanes on nanoemulsion formation and stability has been investigated[24]. The Ostwald ripening is suppressed by the increase in carbon chain length of oil owing to the decrease of its solubility in water[24]. Nevertheless, the initial droplet size increases with the increase in hydrocarbon alkyl chain length due to the increase in the interfacial tension and oil viscosity. In brief, it is difficult to obtain highly kinetically stable nanoemulsions with remarkably small droplet sizes by low energy methods.

The stability of these nanoemulsions was assessed by following the change in droplet diameters with time of storage at room temperature ( $\sim 25$  °C). The size distributions of nanoemulsions prepared at elevated temperatures have not changed over a week. In addition, nanoemulsions prepared within the experimental O/S region (Figure 6) also remained stable during the same storage

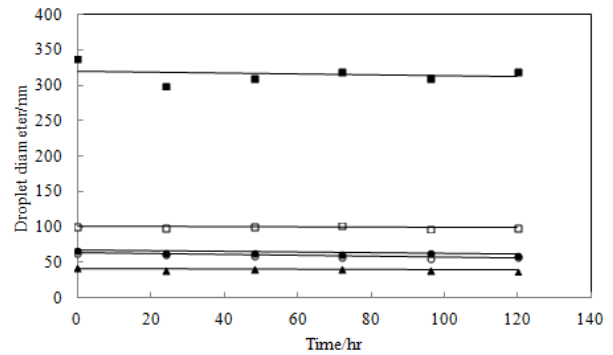


**Figure 7.** Droplet diameter as a function of time for samples with different inner volume fraction of 0.3 (■), 0.2 (□), 0.15 (●), 0.1 (○), and 0.05 (▲) and stored at 25 °C (O/S = 1 : 1).

time. In recent literature it has been presented that the Ostwald ripening rate could be reduced by the addition of a second, less soluble, component to the dispersed phase[20]. In Figure 7, we presented the change of droplet size of different HLB. The size remained constant during the same storage time. It is deduced that the components with long-chain hydrocarbons could help enhance the stability against Ostwald ripening. Figure 8 also shows the effect of droplet volume fraction on the stability of nanoemulsions stored at ambient temperature. Moreover, we assessed the change in droplet size over 2 months. The size of nanoemulsion droplets (Figures 6-8) have not changed over 2 months (Data was not shown). From the above result we concluded that when nanoemulsion composed with less soluble oil was formed, the size remained constant.

#### 4. Conclusion

Paraffin oil-in-water nanoemulsions have been obtained by the PIC method at elevated temperatures. The increase in preparation temperature decreases the droplet diameter of nanoemulsions. The droplet diameter is mainly governed by the structure of microemulsion during the emulsification process. In brief, nanoemulsions could be obtained over a wide range of temperature and droplet



**Figure 8.** Droplet diameter as a function of time for samples with different HLB of 10.5 (■), 11.6 (□), 12.0 (●), 12.6 (○), and 13.1 (▲), and stored at 25 °C (O/S = 1 : 1).

volume fractions. Once formed at elevated temperature, the size distributions of nanoemulsions have not changed over 2 months. The PIC method at elevated temperature is an attractive alternative for preparation of nanoemulsions since this method leads to formation of higher inner phase volume nanoemulsions with long-term stability. These results lead to applying liquid paraffin nanoemulsions in cosmetic vehicles.

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