On the growth mechanisms of nanoemulsions

Elijah Nazarzadeh [a], Tania Anthonypillai [a], Shahriar Sajjadi [a,b,*]

[a] Division of Engineering, ECLAT, King's College London, London WC2R 2LS, UK
[b] Physics Department, King's College London, London WC2R 2LS, UK

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ABSTRACT

The shelf stability of nanoemulsions made by ultrasound, phase inversion composition, and the Ouzo effect was studied using a range of hydrocarbons, as the model oils, and surfactants. The cube of the average drop radius of the nanoemulsions displayed a linear increase with time. Both Ostwald ripening and coalescence can exhibit such behaviour. A new approach, based on the time evolution of drop size distribution, is proposed for unravelling the aging mechanism of nanoemulsions. Sequences of fall and rise in the average drop size of nanoemulsions were clearly observed. The decrease in the drop size could unambiguously be attributed to Ostwald ripening, but the increase could be due to either Ostwald ripening or coalescence/flocculation. Coalescence was identified as the dominant growth mechanism at low surfactant concentrations evidenced by drop size distribution broadening with time associated with the rise in the average drop size. Ostwald ripening was the dominant mechanism at higher surfactant concentrations where the drop size distributions broadened with time during the falls and narrowed with time during the rises of the average drop size. The nanoemulsions produced via the Ouzo process, displayed a coalescence-dependent transient stage and an Ostwald ripening dominated asymptotic regime in the absence of surfactant. The nanoemulsion produced via phase inversion was found to be the most stable one, however, still showed vulnerability to Ostwald ripening and flocculation in the long term.

1. Introduction

Emulsions have found a wide range of applications in many industries including food, cosmetics and pharmacy. While the stability of emulsions is of prime importance for these industries, emulsions are thermodynamically unstable due to their spontaneous tendency toward minimising the interfacial area between phases. For nanoemulsions, having higher interfacial area than macroemulsions, this tendency is even stronger. Due to their small drop size, however, nanoemulsions are less prone to phase separation and are kinetically more stable.

There are various methods available for producing nanoemulsions. Based on the energy consumption, they can be categorised as high-energy and low-energy emulsification methods [1,2]. High-energy methods involve mechanical energy inputs that can be achieved by a high-shear stirrer, ultrasound generator or high-pressure homogeniser. These emulsification methods apply energy to rupture drops in the presence of surfactant which serves to reduce the interfacial tension (typically in the range of 1–10 mN/m). Low-energy methods make use of the chemical potential of the emulsion components [3]. The Ouzo effect, phase inversion temperature (PIT) and phase inversion composition (PIC) are examples of low-energy methods [4]. These emulsification methods (also known as spontaneous emulsification) take advantage of very low interfacial tensions, typically in the range of 0.01–0.10 mN/m, achieved by formulation designs [5]. The nucleation of oil drops in the medium supersaturated with the oil, as a result of a decrease in the solubility of the oil in the medium, has been reported as the main mechanism for drop formation in these methods [5–8]. The nanoemulsions resulting from the low-energy emulsification methods usually have small drops and sharp drop size distributions [4].

Emulsions degrade via two well-known distinctive irreversible demulsification processes: coalescence and Ostwald ripening. Drops grow by the former due to collision with other drops, but by the latter via diffusion of the dispersed phase through the continuous phase because of difference in the chemical potential of drops at different radii [9–11]. Kelvin equation describes chemical potential as

$$c(r) = c_\infty exp\left[\frac{2\sigma M}{\rho_d rRT}\right] \tag{1}$$

where c_∞, σ, M, ρ_d, r, R, and T are the bulk solubility of the disperse phase in the continuous phase, interfacial tension, molar mass, density of the dispersed phase, drop radius, gas constant and absolute temperature, respectively.

* Corresponding author at: Department of Physics, King's College London, London WC2R 2LS, UK. Fax: +44 0207848 2932.
E-mail address: shahriar.sajjadi-emami@kcl.ac.uk (S. Sajjadi).

In an emulsion with drops at different radii, the smaller drops, having higher chemical potential, diffuse to the larger ones. For an emulsion undergoing Ostwald ripening at any given time, there is a critical drop radius (r_c) for which the change in the population of drops is negligible [12]. The critical drop radius can be closely approximated by the number-average radius (r_n) of drops in the emulsion [13]. Lifshitz and Slyozov [14], and Wagner [15] proposed a theory, referred to as LSW theory, for predicting the rate of Ostwald ripening (ω):

$$\omega = \frac{dr_c^3}{dt} = \frac{8Dc_\infty \sigma M}{9\rho_d^2 RT} \tag{2}$$

where D is the diffusion coefficient of the disperse phase in the continuous phase. It should be noted that this theory, which correlates the growth rate to the cube of the critical drop size, is an asymptotic solution ($t \to \infty$) to a more general equation [16]. D can be calculated via the correlation given by Wilke and Chang [17]

$$D = 7.4 \times 10^{-12} \frac{(\phi_s M)^{0.5} T}{\mu V^{0.6}} \tag{3}$$

in which μ and ϕ_s are viscosity of the dispersed phase and a dimensionless factor, respectively. The latter allows for the association between the solvent molecules, which is 2.6 for water, to be taken into account [13].

Eq. (2) predicts a significant dependence of the Ostwald-ripening growth rate on the solubility of the dispersed phase in the continuous phase. Higuchi and Misra [18] have proposed that the addition of an insoluble component to the dispersed phase can eliminate (or lessen) the growth rate caused by Ostwald ripening. The insoluble component is usually known as ultra-hydrophobe [19].

In most previous studies on nanoemulsions only one coarsening mechanism has been considered [20–23]. These studies reported Ostwald ripening as the main demulsification mechanism evidenced by a linear change in the cube of the average drop radius with time. Recent studies pointed to the possibility of coalescence in the nanodispersions made in the absence of surfactants [24,25] and the possibility of flocculation in the nanoemulsions produced in the presence of non-ionic surfactants via the phase inversion composition method [1,7]. For coalescence driven systems, such as highly concentrated macroemulsions, the inverse of the average drop surface area ($1/r^2$) changes linearly with time [26]. This correlation assumes that the frequency of drop collisions is independent of the size of drops, which is an oversimplification for the motion of nanodrops. However, it has been frequently used to examine the probability of coalescence in nanoemulsions [27].

Before two drops can coalesce, they have to move toward each other. The driving forces for the drop motion in nanoemulsions at rest are the gravity and Brownian motion, depending on the size of drops. Submicron drops are only slightly influenced by gravity and hence they largely undergo coalescence via Brownian mechanism. Wang and Davis discussed that the time scale for Brownian-motion induced coalescence is proportional to the cube of the average drop radius (r^3) [28]. This suggests that a linear growth rate of drops with time should not be treated as a conclusive evidence of either Ostwald ripening or coalescence. This dilemma cannot be resolved by referring to the drop size variations either because both degradation mechanisms can lead to an increase in the average size of drops. In the light of this finding, any new investigation should come up with a methodology to distinguish between effective degradation mechanisms.

In this research, we analyse degradation mechanisms of nanoemulsions made by several methods based on the information embedded in their drop size distributions (DSDs). A series of experiments was conducted using sonication as a high-energy emulsification method, and the Ouzo process and phase inversion emulsification as low-energy methods. A set of alkanes with different chain lengths (hexane, octane, decane, dodecane, tetradecane, and hexadecane) and physical properties (as listed in Table 1) was used as model oils to produce nanoemulsions. Sodium dodecylsulfate was used as an anionic surfactant in the sonication and the Ouzo methods and a mixture of Tween20/Span80 was used as non-ionic surfactants in the PIC method.

2. Experimental

2.1. Materials

Sodium dodecylsulfate (SDS), Tween20 and Span80 were obtained from Sigma–Aldrich and was of 99% purity. The alkanes, hexadecane ($C_{16}H_{34}$; C16), tetradecane ($C_{14}H_{30}$; C14), dodecane ($C_{12}H_{26}$; C12), decane ($C_{10}H_{22}$; C10), octane (C_8H_{18}; C8), and hexane (C_6H_{14}; C6) were obtained from Sigma–Aldrich. Ethanol was obtained from VWR and was of 99.9% purity. De-ionised water was obtained from an ELGA PURELAB Option water purification system. All of the chemicals were used as received.

2.2. Apparatus

A digital sonifier model 450 from Branson Ultrasonics Corporation with the maximum output of 400 W (with frequency of 19.850–20.050 kHz) was used for producing nanoemulsions.

2.3. Measurement

Dynamic light scattering (Nanosizer ZS; Malvern Instruments) at a fixed scattering angle of 173° and with laser wavelength of 633 nm was used for measuring the average drop size and drop size distribution (DSD) of emulsions. In order to evaluate the reliability of the DSD data produced by Nanosizer, silicone oil nanoemulsions with different mean drop sizes were produced and then mixed together with different ratios to produce model nanoemulsions within a wide range of drop sizes. The size distributions of model nanoemulsions were then compared with those of the constituent nanoemulsions. The test results clearly indicate that while the overall DSD cannot always reproduce the individual ones quantitatively, but could capture almost the entire distribution and show, at least qualitatively, the bimodality or skewness of the distributions when the size distribution is not very wide (see Supplementary data, Fig. S-3). The frequency of the smaller peak, in a bimodal distribution, was significantly underestimated if the size difference between the means of the two peaks was more than 3 times. Oil/water interfacial tension in the presence of surfactant was measured by the pending drop method using FTA200 tensiometer.

2.4. Methods

Ultrasound: Emulsions were produced under isothermal conditions (at 17.0 ± 2.0 °C) using a jacketed vessel. The sonifier was set to work for 2 s of active sonication intervals followed by 20 s pauses. Total active sonication time was 180 s. The amplitude was kept constant at 70%.

Ouzo effect: 5.0 ml of 0.1 vol.% oil in ethanol solution was added to 10.0 ml of water being stirred at room temperature.

Phase inversion composition: A solution of 70 wt.% Tween20/Span80 in hexadecane was prepared and then gradually diluted with pure water, while being stirred by a magnet stirrer at room temperature, at the addition rate of 0.1 ml/min. The surfactant