Development of Curcuminoids Oil Nanoemulsions Produced by High-Energy Methods: Microfluidization *vs* Ultrasonication

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ABSTRACT

This study aimed to compare two high-energy emulsification methods to produce curcuminoids nanoemulsions. Emulsions were produced using a microfluidizer, and an ultrasonic processor. The droplet size and polydispersity index of the emulsions were measured using a dynamic light scattering equipment. Microfluidization process produced a droplet size of 128 nm with a polydispersity index of 0.37, respectively. On the other hand, after 30 min of ultrasonication, nanoemulsions had a droplet size of 99 nm with a polydispersity index 0.17. Ultrasonication was an efficient technique to generate nanoemulsions than microfluidization.

Keywords: Turmeric, nanoemulsions, ultrasonication, microfluidization, droplet size, polydispersity.

1 INTRODUCTION

Turmeric curcuminoids are phytopolylphenol pigments of *Curcuma longa* root used due to their bright yellow-orange shades and to their antioxidant, anti-inflammatory, antiviral, antibacterial, antifungal, and anticancer activities [1]. Commercial samples contain curcumin (~77%), demethoxycurcumin (~17%), and bisdemethoxycurcumin (~3%) as its major components [2]. These water-insoluble compounds are highly sensitive to pH, light, and oxygen [3]. Their low solubility and low bioavailability are improved using emulsifiers agents as surfactants (tweens or lecithins), proteins (milk or soy proteins), or polysaccharides (gum Arabic) [4]. Lecithins are a natural mixture of phospholipids dissolved in oil with a low incidence of allergic reactions. These can be used to produce nanoemulsion with small droplet size and longer shelf life [5].

Several regulatory agencies around the world coincide that the nanomaterials have particle sizes in the range of 1 nm to 100 nm [6] But also, can include those materials outside of nanoscale (> 100 nm) that exhibit similar functional effects than nanomaterials, *e.g.*, increased bioavailability, decreased dosage, or increased potency of a drug product, reduced the toxicity of a drug product, among others.

Typically, the energy necessary to produce a nanoemulsion is of the order of 10-10^2 kJ/m^3. This energy is supplied by high-pressure homogenization, microfluidizers, or ultrasonication. Microfluidizer is a continuous process, in which a low viscosity fluid is forced through a homogenization chamber at high pressures (50–400 MPa), where intense shear, elongation stresses, turbulence, and cavitation are developed. The energy supplied by microfluidizer is around of 10^4-10^6 kJ/m^3. On the other hand, the ultrasonication process applies sound waves of high frequency into the sample using a sonotrode tip producing a mechanical vibration and acoustic cavitation that breaks the emulsion droplets. The energy supplied by ultrasonication is around of 10^3-10^5 kJ/m^3 [7]. Several reports showed that the droplet size of emulsions decreased with increasing ultrasonication time, input energy and surfactant concentration.

This study aimed to compare two high-energy emulsification methods (microfluidization and ultrasonication) to produce curcuminoids nanoemulsions.

2 METHODOLOGY

2.1 Materials

Curcuminoids powder was purchased from future foods (Mexico). Hydroxylated soy lecithin Emulfluid HL 66 was obtained from Lallemand Mexico (Mexico). Medium chain triglycerides were purchased from Gomas Naturales (Mexico).

2.2 Emulsions

The curcuminoids oil phase (10 mg/mL) was prepared according to the procedure described by Ochoa et al. [8] We used a two-stage emulsification process for making nanoemulsions. A coarse emulsion (volume oil phase = 0.1) was prepared using a high-speed mixer (Silverson, L5M, UK) at 4000 rpm for 2 min. In the second stage of the emulsification process, the coarse emulsion was homogenized using a microfluidizer M-110 PS at 20000 psi for 10 passes (NP) (Microfluidics International Corporation, USA). Also, the coarse emulsion was homogenized for 30 min using an ultrasonic processor VCX 750 PB (Sonics &

Materials, Inc., Newtown CT.) using a 13 mm stainless steel probe and an amplitude of 90%.

2.3 Dynamic light scattering (DLS)

The droplet size and polydispersity index (*PdI*) of the emulsions were measured using a Zetasizer Nano ZS90 (Malvern Instrument, UK). The Stokes-Einstein equation calculated the emulsion droplet size:

$$DS = k_B T / 3\pi \eta_s D \quad (1)$$

Where k_B is the Boltzmann constant, T is the temperature (K), η_s is the viscosity of the solvent and D is the Z-average translational diffusion coefficient. Each emulsion was diluted at a concentration of 0.01 g/mL in deionized water. All measurements were made in a glass cuvette at 20 °C. The polydispersity index was used for comparative purposes, *i.e.*, broader distributions, PdI ≥ 0.5; monomodal emulsions, *PdI* < 0.2 [9]. The values reported were measured in triplicate of each experimental run.

3 RESULTS

The coarse emulsion produced by high shear mixer showed a droplet size of 2.38 ± 0.55 μm with a higher polydispersity index (> 0.5). High energy was required to decrease the droplet size under the nanosize. In the microfluidization process, we pass the emulsion several times through the microfluidizer chamber to reduce the droplet size of the emulsion (Figure 1). After only one pass, the droplet size has been reduced to 180 nm and become less polydisperse (*PdI* = 0.21). After ten successive passes, the droplet size of the emulsion was of 128 nm. Polydispersity index increased slightly after the four passes from 0.24 to 0.38.

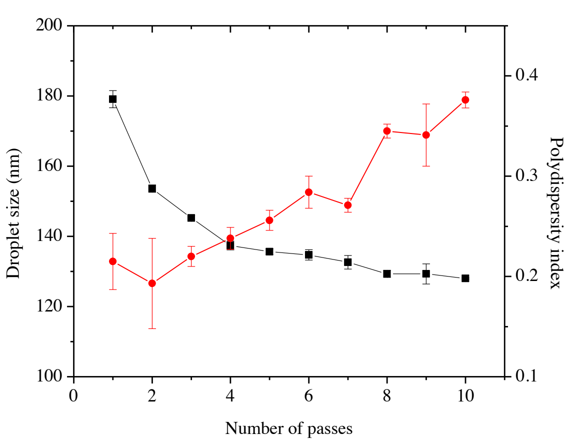

Figure 1: Droplet size and the polydispersity index of emulsions produced by microfluidization as a function of the number of passes.

The reduction of microfluidization droplet size (DS_M) was adjusted to the potential law:

$$DS_M = 172.25\ NP^{-0.29} \quad (2)$$

Where, *NP* is the number of passes through the microfluidization chamber. This empirical model shows that the droplet size of the emulsion varies roughly as the inverse of the cube root of the number of passes.

On the other hand, ultrasonication was very efficient in size reduction due to the narrow distance between the tip of the sonotrode. After two minutes of ultrasonication, the droplet size was reduced to 220 nm. Ultrasonication times of 26 min were required to producing nanoemulsions (< 100 nm) with a lower polydispersity index (< 0.15). In this condition, the total energy applied was 46.8 kJ/mL.

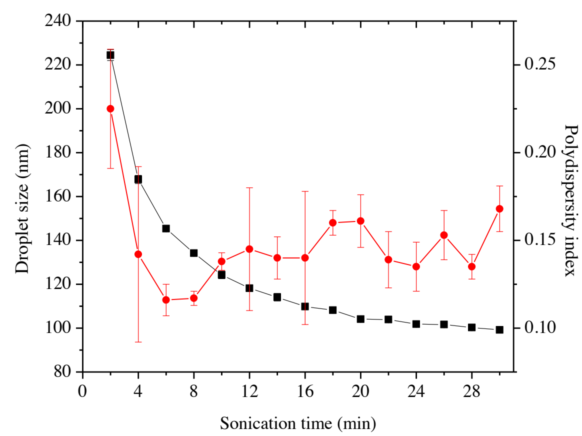

Figure 2: Droplet size the polydispersity index of emulsions produced by ultrasonication as a function of time. Power of 750W & amplitude of 90%.

The ultrasonication droplet size (DS_U) was adjusted to the potential law:

$$DS_U = 252.62\ t^{-0.29} \quad (3)$$

Where, t is the sonication time in minutes. Li et al. [10] and Gupta et al. [11] reported power-law indices of -0.8 for sunflower oil/SDS emulsions. The ultrasonication achieved nanosize droplets and less polydisperse than those obtained by the microfluidization (Figure 3).

Figure 4 shows the optical appearance of curcumin emulsions produced by high energy methods and high shear mixer. The coarse emulsion exhibited a yellow-ochre color, whereas the high-energy emulsion exhibited a bright-light yellowish color. Notably, the nanoemulsion produced by ultrasonication showed translucent appearance.

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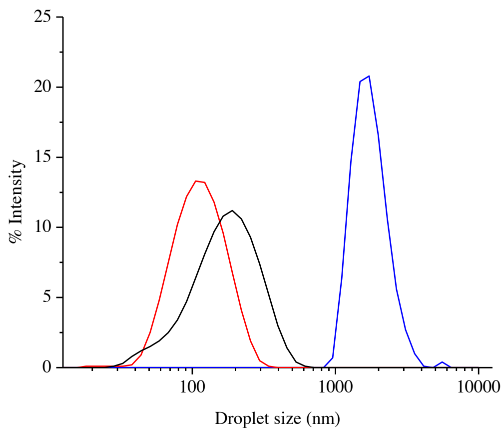

Figure 3: Droplet size of emulsions make by microfluidization (– black line), ultrasonication (– red line), and high shear mixer (– blue line).

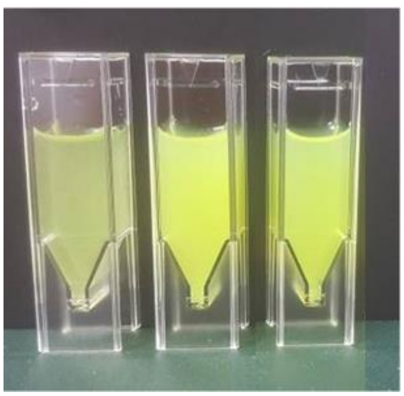

Figure 4: Curcuminoids oil nanoemulsions: (a) coarse emulsion, (b) microfluidization nanoemulsion, and (c) ultrasonication nanoemulsion.

4 CONCLUSION

The microfluidization and ultrasonication techniques generate fine emulsions with narrow distributions. Inverse power law model is describing the emulsion droplet size reduction for both technologies. Increasing the time of ultrasonication decreases the droplet size, while the increasing the number of steps reduce the droplet size of the emulsion. Ultrasonication was an useful technique to produce nanoemulsions.

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