Journal of Molecular Liquids 220 (2016) 604–622

Contents lists available at ScienceDirect

Journal of Molecular Liquids

journal homepage: www.elsevier.com/locate/molliq

Physicochemical study of curcumin in oil driven nanoemulsions with surfactants

Parth Malik [a], R.K. Ameta [b], Man Singh [b,*]

[a] Centre for Nano Sciences, Central University of Gujarat, Gandhinagar 382030, India
[b] School of Chemical Sciences, Central University of Gujarat, Gandhinagar 382030, India

ARTICLE INFO

Article history:
Received 16 December 2015
Accepted 30 April 2016
Available online xxxx

Keywords:
Brownian scale
Isentropic compressibility
Acoustic impedance
Nanoemulsions
Dispersed
Walden's hypothesis

ABSTRACT

Physicochemical profile for 0.220 to 1.099 μmol·kg^{-1} curcumin at 0.220 μmol·kg^{-1} interval, dispersed in homogenized nanoemulsions of (cottonseed oil + surfactants (sodium dodecyl sulphate-anionic, dodecyltrimethylammonium bromide-cationic, poloxamer-407 and tween-20–nonionic) + hydrophilic additives (ethanol, glycerol)) at Brownian scale, from (298.15 to 308.15) K is reported. State of medium binding forces for absolute dispersion has been investigated *via* sound velocity, isentropic compressibility, acoustic impedance, electrical conductivity, particle size and zeta potential. Positive Gibbs energy, negative entropy changes and enthalpies with high reproducibility have inferred thermodynamically and kinetically stable emulsions. The −144.21 to 149.60 mV zeta potentials and (1300–1600, 2800–3100 and 3513) cm^{-1} Fourier Transformation Infra-red (FTIR) stretching frequencies have confirmed stability, intramolecular hydrogen bonding, a presence of carbon-carbon bonding and the phenyl ring on stabilized micelle formation with curcumin. An agreement of Walden's Hypothesis for curcumin formulations signified a distribution of molecular forces in philicphobic driven nanoemulsions *via* intramolecular multiple force theory.

1. Introduction

For few years, screening the medicinal characteristics of natural polyphenolic compounds has attracted a significant scientific attention, attributed to their structurally hydrophobic nature, encouraging an administration *via* altered routes [1–5]. Thereby, surfactant engineered emulsions have advanced as interesting smart vehicles, with capabilities of inducing additive effects from the chemical modulators to ascertain properties of functional molecules [6–8]. The surfactants make the emulsions structurally robust, owing to availability of polar ionic groups as well as of non-polar hydrophobic chains. Such features make emulsions the ideal candidates for an effective transformation of the cohesive forces (CFs) in rigid hydrophobic compounds into intermolecular forces (IMFs) for a uniform dispersion. In general, emulsifiers are selected on the basis of their potential to stabilize the dispersed phase; thereby a selection of an emulsifier affects the oxidative stability of encapsulated bioactives to impart special abilities to philicphobic modulated micellar systems as efficient drug-delivery vehicles [9–11]. Amongst the emulsions, nanoemulsions are emulsions with minimal interactions of philicphobic components to enable an efficient transport and delivery of hydrophobic compounds at critical physiological locations, owing to their exceptional kinetic stabilities [12–14]. Several attempts for optimizing nanoemulsions as efficient drug carriers have employed nonionic surfactants owing to their comparatively low water solubility and less stringent constraints for pH monitoring [15–17].

For an evaluation of composition specific structural performance of nanoemulsions, a systematic and logical analysis of temperature sensitive physicochemical properties is currently an essential prerequisite. The distinct physicochemical probes enable an efficient screening for biotechnology and pharmaceutical relevance since a pilot scale study requires wider applications as per the situation, so all the probes could not be applicable to all the situations. Further, these inputs also ascertain the intensity of interactions and not reactions, where such probes require a careful selection for a minimum structural attenuation of the dispersant [13,18–19]. Additionally, a systematic study of temperature dependent physicochemical properties (PCPs) could be useful to understand an impact of molecular and geometrical alterations during interactions from a physiological point of view [20–22]. Under such a scenario, the choice of structurally coherent and compatible stabilizers could facilitate apt structural activities for an effective dispersion resulting in an entropic rather than enthalpic modulation [23–25], since the former enables a structural intactness. Also, constant molecular reorientations controlled *via* intramolecular multiple force theory (IMMFT) [26] operating through definitive intramolecular entropies and Boltzmann energy distributions could be crucial in shaping up the active force gradients to drive an efficient structural performance. Till date, several studies have reported an improved functional activity of curcumin (curc) through nanoemulsions, ascertained mainly *via* only

* Corresponding author.
E-mail addresses: parthmalik1986@gmail.com (P. Malik), ametarakesh40@gmail.com (R.K. Ameta), mansingh50@hotmail.com (M. Singh).

http://dx.doi.org/10.1016/j.molliq.2016.04.126
0167-7322/

particle size, zeta potential, centrifugation or microscopic analysis [27–35].

Therefore, present study reports the sound velocity, isentropic compressibility, conductivity, zeta potential, acoustic impedance, physical validation and FTIR spectra for curc nanoemulsions with variable surfactants at 298.15, 303.15 and 308.15 K. Earlier we reported detailed studies on DPPH• free radical scavenging activities (RSAs) for curc depicted *via* density, surface tension, viscosity and UV/Vis spectroscopy [36]. For ascertaining the role of degrees of freedoms out of all physicochemical arrays, the scarcity of correlative biological-physicochemical evidences has created an urgent need for exploring possibilities of using said PCPs to ascertain curc dispersion. Further, to the best of our knowledge, a detailed account of thermodynamic variance of aforementioned PCPs has never been reported to justify specific structural dynamics of curc. The latter assumes even more significance considering the fact that the curc is an unstable molecule with susceptible stability towards light, pH and temperature [37,38]. Therefore, it becomes very essential that curc retains its physicochemical properties and stability upon encapsulated in nanoemulsions. The information generated out of this study may enable a rationalistic design of delivery systems for an improved expression of curc structural potentials and other health beneficiary lipophilic compounds. Therefore, further advancement in the quality of nanoemulsions could be made using poly-ethylene glycol (PEG) stabilized dendrimers, carbohydrates, zwitterionic structures and salts. This is because PEG-dendrimers, carbohydrates and zwitterions do have several electrostatic sights with moderate binding abilities towards oil in aqueous medium, and such multifaceted binding sites enhance the thermodynamic and kinetic stability by preventing agglomeration and coalescence. With such attributes, nanoemulsions of high stability and moderate polydispersity index (PDI) could serve as excellent dispersion medium for curc.

2. Experimental

2.1. Materials

Tables 1A and 1B comprises the names, sources, purity levels, chemical nature and CAS numbers of analytical grade reagents, used as received. Milli-Q water of 10^{-7} $S \cdot cm^{-1}$conductivity was used for solution preparation. Glassware was cleaned and dried to absolute dryness using standard methods.

2.2. Methods

2.2.1. Preparation of emulsions

The (0.0007, 0.0013, 0.0020, 0.0027 and 0.0033) $mol \cdot kg^{-1}$ cottonseed oil (heated to ~70 °C) (Table 2) [39] were separately taken into 100 mL RB flasks with micropipette. Also 0.021 $mol \cdot L^{-1}$glycerol (mass fraction purity 0.99%, Table 1A) and 1.22 $mol \cdot L^{-1}$ethanol were added as co-surfactant and co-solvent respectively. Thereafter, 0.002 m aqueous surfactant solution (except poloxamer-407) was added in each RB for making 35 mL. In case of poloxamer-407, its 0.002% (w/w) solution was added. The resultant mixtures were kept for magnetic stirring at 650 rpm at room temperature (RT) for 45 min.

Table 1A
Sources and purities of reagents used in study.

Sr. no.	Name	Source	Mass fraction purity[a]	CAS no.
1.	Sodium dodecyl sulphate	Sigma-Aldrich	0.9980	151-21-3
2.	Dodecyltrimethylammonium bromide	Sigma-Aldrich	0.9990	11119-94-4
3.	Poloxamer-407	Sigma-Aldrich	0.9960	11-6-9003
4.	Tween-20	SDFCL	0.9975	9005-64-5
5.	Curcumin	Sigma-Aldrich	0.9438	458-37-7
6.	Glycerol	Sigma-Aldrich	0.9958	56-81-5
7.	Ethanol	Sigma-Aldrich	0.9889	64-17-5
8.	2,2-Diphenyl-1-picrylhydrazyl	Sigma-Aldrich	0.9999	1898-66-4

[a] As provided by supplier.

Table 1B
Individual constituents of blank and curcumin loaded formulations (CLFs).

Sr. no.	Blank formulations	CLFs
1.	Oil (0.0007, 0.0013, 0.0020, 0.0027 and 0.0033) $mol \cdot kg^{-1}$	Oil-curcumin mixture carrying (0.0010, 0.0019, 0.0029, 0.0038 and 0.0048) $mmol \cdot kg^{-1}$ oil and (0.220, 0.440, 0.659, 0.879 and 1.099) $\mu mol \cdot kg^{-1}$ curc
2.	Ethanol (1.22 $mol \cdot L^{-1}$)	Ethanol (1.22 $mol \cdot L^{-1}$)
3.	Glycerol (0.021 $mol \cdot L^{-1}$)	Glycerol (0.021 $mol \cdot L^{-1}$)
4.	0.002 m aq. surfactant (for poloxamer-407, 0.002% (w/w) solution was used)	0.002 m aq. surfactant (for poloxamer-407, 0.002% (w/w) solution was used)

2.2.2. Curcumin encapsulated nanoemulsions

Initially, 3 mM curc solution was prepared in warm cottonseed oil at ~70 °C (composition detailed in Table 2)through magnetic stirring at 1000 rpm. Thereafter, as per the compositions described in Table 1B, we prepared curc loaded formulations (CLFs) carrying (0.220, 0.440, 0.659, 0.879 and 1.099) $\mu mol \cdot kg^{-1}$ curc, respectively. The concentrations of curc have been computed using densities of oil and oil-curc mixture at (298.15, 303.15 and 308.15) K (Table S1, Supporting information) [36]. The procedure for making CLFs was similar to that adopted for making blank formulations.

2.3. Experimental measurements

2.3.1. Physicochemical and conductometric characterization

Solutions (w/w) were prepared using Mettler Toledo New Classic MS with an inbuilt self-calibrator of $\pm 1 \times 10^{-4}$ g accuracy. Densities (ρ) and sound velocities (u) were measured using an Anton Paar Density and Sound Velocity meter, DSA 5000 M, having $\pm 1 \times 10^{-3}$ K temperature controlled *via* built-in-Peltier device and $\pm 5 \times 10^{-6} g \cdot cm^{-3}$ and $1 \times 10^{-2} m \cdot s^{-1}$accuracies, respectively. The Anton Paar measures oscillation periods of quartz U tube with air, solvent and solutions [40–44]. For each measurement the sample holding tube was cleaned with acetone and dry air using an air pump. The drying was continued till a constant oscillation period similar to that of initial calibration was obtained. For measurement of u, the instrument passes ultrasonic waves through a sample *via* a transducer at a frequency of 3 MHz, which are analyzed by receiver after travelling ≈5 mm. To ensure precision, about five–six measurements were made, corresponding to each sample. A comparison between the literature and experimental values of density (ρ) and sound velocities (u) of pure water with standard deviation at T = (298.15, 303.15 and 308.15) K is given in Table S2 (Supporting information) which shows accuracy and calibration of the instrument.

Conductivities for blank and CLFs were measured with the LABINDIA, PICO + model conductivity meter at (298.15, 303.15 and 308.15) K. The instrument works on alternating current of frequency (47–63) Hz at a potential difference of (100 − 300) volts and has an accuracy of 0.5%. The calibration of the conductivity meter was made using aqueous 0.1 M (12.88 $mScm^{-1}$), 0.01 M (1.413 mS cm^{-1}) and 0.001 M (0.147 mS cm^{-1}) KCl solutions at 298.15 K. For each measurement, seven values were taken at a particular temperature and thereafter, the mean was computed.

2.3.2. Zeta potential measurements

Zeta potentials for aqueous surfactants, aqueous surfactants with ethanol and glycerol and the CLFs have been measured with Dynamic Light Scattering (DLS, *MicrotracZetatrac*, U2771). The set-zero was made using aqueous surfactant containing ethanol and glycerol to