Study of the influence of the viscosity of microemulsified systems on the sizes of the internal phase

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Abstract

Based on oral W/O ranitidine hydrochloride-containing microemulsions, we studied (i) the influence of the viscosity of the external phase on the mean size of dispersed phase and (ii) the correlation between these two parameters. Viscosity measurements were carried out with rotating cylinder geometry. The sizes of the droplets were determinated by Dynamic Light Scattering at various fixed values of viscosity and refractive index. Conclusions of this study were that (i) the determination of the viscosity is necessary to characterize physically the systems and to control their stabilities and (ii) the mean particle sizes are highly dependent on the viscosity of the system.

Introduction

Dynamic Light Scattering (also known as **PCS - P**hoton **C**orrelation **S**pectroscopy) measures **Brownian motion** and relates this to the size of the particles. It does this by illuminating the particles with a laser and analysing the intensity fluctuations of the scattered light [1].
It is virtually impossible to determine diameter of particles without knowledge of continuous phase viscosity and index of refraction. We analysed a situation when we do not know the composition of continuous phase - such microemulsion is complex system and composition of continuous phase cannot be analyzed in anyway. We have tried to bypass this problem doing measurements at various fixed values of viscosity and refractive index, hoping that at some values we will get physically reasonable results.

Materials and methods

Materials

Ranitidine hydrochloride was a gift of Sochibo (France). Propyl gallate (antioxidizing agent) and p-hydroxybenzoic acid methyl and propyl esters (preservative agents) were gifts from Unipex (France). Sodium cyclamate was gift from Arnaud Group (France). Montanox® 80 was obtained from Seppic.

Methods

Dynamic light scattering (DLS) measurements as follows
Our acquisition/calculation program allows introduction of parameters as shown below. In some cases we have fixed index of refraction (1.455 or 1.465), changing viscosity (most common), while in some cases we evaluated effect of variable index of refraction at constant viscosity.
Typical measurement modus was the following: value of refractive index was entered, followed by some value of bulk viscosity, and then measurement has been taken. Results obtained were recorded, value of viscosity changed, and measurement repeated at constant index of refraction. Typically, approximately 12 measurements have been recorded, and results placed in the graphs as shown in Figures 1-3.

Instrumentation

DLS measurements were carried out with a Nicomp ZLS 380 (Nicomp Inc., Santa Barbara CA, USA), working in heterodyne mode. Light source was 50 mW diode, emitting at 532 nm; the scattering angle was fixed at 90 degrees. Temperature was maintained at 23°C using built-in Peltier device. Data were acquired and processed by means of ZW380 software. Channel width, sensitivity and baseline adjustment has been determined automatically. Both viscosity and index of refraction of continuous phase were entered manually. Results have been fitted by means of Gaussian model, assuming monodispersity of the sample.

Experimental procedure

Approximately 3.5 mL of sample was taken into standard plastic UV cuvette (40×10×10 mm) using sterile polypropylene syringe (standard medical type). Two series of measurements, 7.5 min. each, have been taken, and averaged by software

Results and discussion

1. Fixed index of refraction (1.455 or 1.465), variable viscosity.

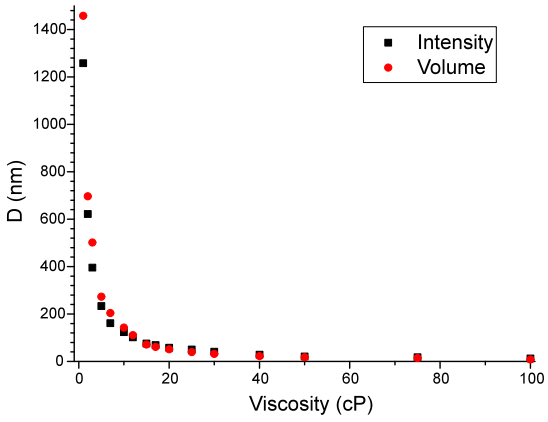

Fig.1: Constant refractive index n = 1.47, variable viscosity
Measurement 1×5 min for each point. Results: for η = 8.2 cP: 180.8 nm (volume), 148 nm (intensity).

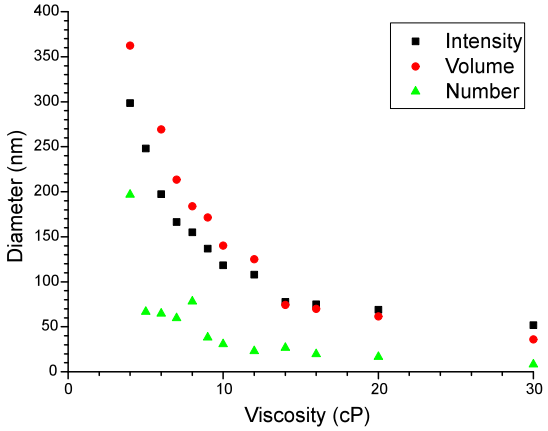

Fig.2: Constant refractive index n = 1.455, variable viscosity

For η = 8.2 cP calculated diameter was 182.5 nm (volume) and 151.3 nm (intensity).

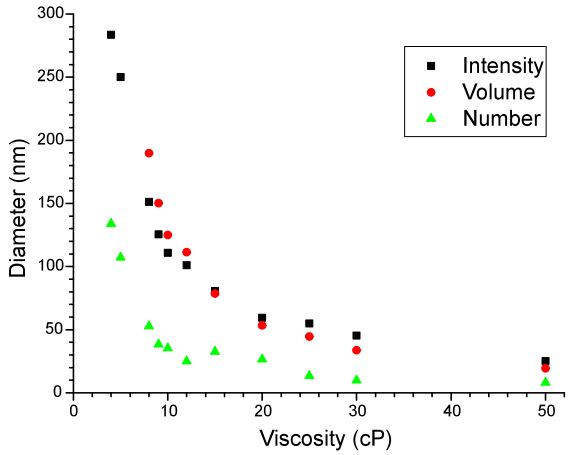

Fig.3: Constant refractive index n = 1.465, variable viscosity
For η = 8.2 cP calculated diameter was 185.7 nm (volume) and 148 nm (intensity).

2. Constant viscosity, variable refractive index

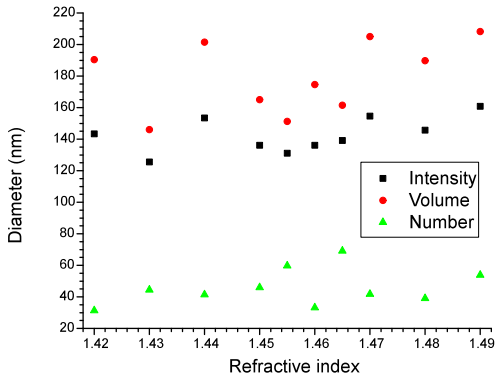

Fig.4: Constant viscosity η = 8.2 cP, variable refractive index
Average value of D was 142.6 ± 11.2 nm (intensity), 179.3 ± 22.8 nm (volume).

One can interpret the graphs in following way: **if** the viscosity of continuous phase is equal to some value, **then** corresponding diameter can be read from the graph. Without knowledge of viscosity one **can not** determine hydrodynamic parameters of dispersion.
In order to check an effect of refractive index of bulk phase on hydrodynamic radius, one series of measurements has been recorded at constant viscosity (8.2 cP) with the value of refractive index changed before each measurement.
It seems that change of the refractive index results in some fluctuations of the results; however these changes are quite random. Some average value of diameter can be estimated.
Results can be smoothly fitted using first-order inverse function:

$$D = D_0 + \frac{a}{\eta}$$

where D is the diameter of particle, η is the viscosity, D_0 and a are the parameters of regression equation.

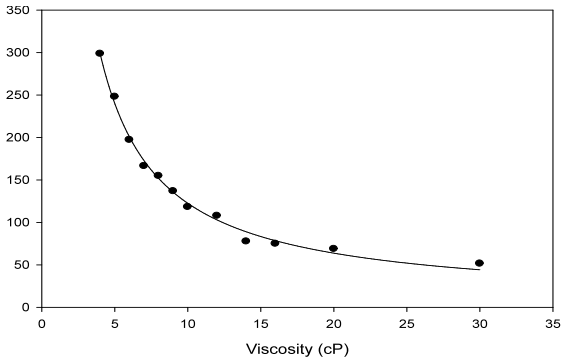

Fig.5: Results of the regression for intensity value for the constant index of refraction, n = 1.455.

Another interesting observation has been done. The curve of D = f (η) can be fitted with two lines, one for η→ 0, and another for η → ∞ (fig.6). Cross-section of these lines gives us some value of viscosity lying around 11-13 cP, depending on measurement method and index of refraction.

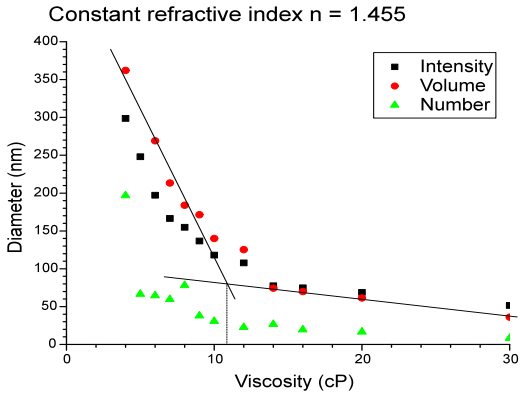

Fig.6: Diameter of droplets versus viscosity of microemulsion D = f (η)

This cross-point can have some physical sense (fig.6); however, when we have measured particles of titanium dioxide in water and ethylene glycol [2], these lines crossed at *ca.* 1 and 20 cP, respectively, which is close to the literature values of viscosity for above liquids.
There is no reliable method to determine hydrodynamic parameters of this emulsion. To solve the problem, diameter of droplets must be measured microscopically or viscosity of continuous phase determined using fluorescence spectroscopy. Hydrophobic excimer probe, like 1, 3-dipyrenylopropane should provide accurate information on microviscosity of the system, and subsequently give rise to hydrodynamic radius.

Conclusion

We tried determining convincingly the hydrodynamic radius of microemulsion droplets. The problems arise from relatively high optical density of the system at 532 nm (wavelength of the laser), which results in partial absorption of the laser beam, as well as scattered light. Such absorption leads to local heating of the sample, and change of diffusion coefficients. Paradoxically low-power laser used seems to give more reliable results than high power ones – heating of the sample is much lower than in the case of more intensive beams, while intensity of scattered light is high enough to perform some measurements, albeit with difficulties, resulting in substantial error level.

Bibliography

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