Vesicles as rheology modifier

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Abstract

Vesicles are self-assembled spherical aggregates of amphiphilic molecules with rich structural variety. They have attracted increasing attention due to their possible applications in pharmaceutics and cosmetic fields, but also from a more fundamental point of view. In this work, we present vesicle formation from mixtures of commercial surfactants. We show how mixing of two non-ionic surfactants can lead to vesicle formation by adjusting the packing parameter of the mixture. High-frequency viscosity data can be described in terms of an effective hard sphere system applying the Lionberger–Russel model. Thus, we were able to estimate the hydrodynamic volume of the vesicles and hence their average size, which agrees well with the structures observed by transmission electron microscopy. Finally, we show that oil-in-water emulsions prepared with the adjusted surfactant mixture have two orders of magnitude higher viscosities compared to similar emulsions stabilised with an anionic surfactant, demonstrating the significant impact of the vesicles on the rheological and hence creaming behaviour of emulsions.

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1. Introduction

Amphiphile molecules (e.g. surfactants, block copolymers) can build a large variety of structures in water. Depending on the amphiphile-type, on its concentration and on external parameters such as temperature or salinity, these structures vary from spherical or rod-like micelles, lamellar or sponge structures to reverse micelles. Knowledge of parameters leading to this wide family of structures is important both for industrial applications and from a more fundamental point of view.

Discovered in the middle of the 1960s [1], vesicles retain increasing attention. They consist of one or more amphiphile bilayer(s) that surround an aqueous core. Their encapsulation properties lead to a wide range of applications including pharmaceutical science [2,3] and cosmetics [4,5]. Vesicles have also been proposed and successfully employed as templates for chemical reactions [6–8]. Furthermore, vesicular structures can also be used as rheology modifier [9].

Vesicles can be formed from different types of amphiphile molecules, cationic vesicles [10], for instance, are made of equimolar mixtures of anionic and cationic surfactants; liposomes [1] are formed from phospholipids, whereas non-ionic surfactants lead to niosomes [4]. Diblock copolymers with similar hydrophilic-hydrophobic properties as surfactants may also form vesicles [11]. Several kinds of vesicular structures have been reported upon in the literature: from ultra-small unilamellar vesicles (USUV), multi-lamellar vesicles (MLV) to giant unilamellar vesicles (GUV). These structures differ in size and number of bilayers forming the shell (Fig. 1).

In this article, we describe vesicle formation from a commercial surfactant mixture that is used within the cosmetic industry. We show how mixing two surfactants can induce vesicle formation by adjusting the mixture’s packing parameter. By applying the Lionberger and Russel model [12] to high-frequency viscosity data, we were able to estimate the
Fig. 1. Different kinds of vesicles [12]. SUV, USUV, LUV, MLV, and GUV correspond to small unilamellar vesicles, ultra-small unilamellar vesicles, large unilamellar vesicles, multilamellar vesicles, and giant unilamellar vesicles, respectively.

average vesicle size, which agrees well with results from electron microscopy measurements.

In order to evaluate the influence of vesicles on the rheological properties of emulsions, we prepared oil-in-water emulsions stabilised with the adjusted surfactant mixture and compared these emulsions with emulsions stabilised with an anionic surfactant (sodium dodecyl sulfate, SDS). While the SDS-stabilised emulsions have viscosities that agree well with the theoretical estimate of emulsions having a 20% volume fraction of the dispersed phase, the emulsions containing vesicles have a two orders of magnitude higher viscosity, demonstrating the significant impact that vesicles can have on the viscosity and in turn, e.g. the creaming behaviour of an emulsion.

2. Materials and methods

Several samples with various concentrations of surfactant were prepared with the following chemicals: Cremophor® A6 and Cremophor® A25 are non-ionic BASF surfactants. Cremophor® A6 is a mixture containing 75% of a poly(ethylene oxide) alkyl ether (C\text{16–18}E\text{6}) and 25% stearyl alcohol. Cremophor® A25 is a poly(ethylene oxide) alkyl ether with longer ethylene oxide chain length (C\text{16–18}E\text{25}). The densities of Cremophor® A6 and Cremophor® A25 are about 0.9 and 1.02 g/ml (60 °C), respectively.

Water and the surfactants were mixed in various compositions at 80 °C under stirring (Heidolph IKA stirrer) at 150 rpm and subsequently homogenised with a T25 Ultra-Turrax at 13,000 rpm for 1 min. The samples were cooled to room temperature under moderate stirring at 150 rpm, and then stored at room temperature.

For the emulsion measurements, 20 vol.% paraffin oil (Riedel-de-Haen) with a viscosity of 230 mPa s was emulsified in water stabilised by a Cremophor® A6/Cremophor® A25 mixture (7:3) and sodium dodecyl sulfate (SDS, 99% ABCR Karlsruhe), respectively.

Transmission electron microscopy (TEM) measurements, as well as optical microscopy experiments were performed. For the investigation of surfactant vesicles in the TEM a small sample droplet is shock frozen in liquid ethane at −183 °C and freeze-fractured in an evaporation chamber. Freeze-etching by ice sublimation at elevated temperature (−120 °C) results in a topographical presentation of the vesicle phase at the fractured surface. This topography is replicated by oblique evaporation of a thin Pt/C layer, which now contains the morphological information of the vesicle. At room temperature the replica is cleaned from adhering surfactant material in a chromic–sulfuric acid mixture and imaged in a transmission electron microscope (freeze-fracture TEM).

Dynamic viscosity measurements were performed at 23 °C with a rotational viscometer (Physica MCR 300, double gap concentric cylinder system according to DIN 54453) covering the shear rate range from 1 to 1000 s⁻¹, with accuracy better than 5%. Small amplitude oscillatory shear experiments in the kHz range were carried out with a torsional resonator (titanium cylinder, f\text{res} = 19 and 57 kHz) [13]. This
allows the measurement of the complex shear modulus $G^*$ ($=G' + iG''$) and the complex shear viscosity $\eta^*$ ($=\eta' + i\eta''$), respectively.

3. Results and discussion

3.1. Microscopy

The weight ratio, $r$, of Cremophor® A6/Cremophor® A25 was varied corresponding to 10:0, 9:1, 8:2, 7:3, and 6:4, and the appearance of the resulting molecular structures was monitored by optical microscopy and TEM (Figs. 2 and 3). In a solution of 1 wt.% Cremophor® A6 (i.e. a mixture of stearyl alcohol and Ceteareth-6), large crystal structures were obtained (with a size $\sim 10–100 \mu m$, Fig. 2a). When Cremophor® A25 was added to Cremophor® A6, i.e. upon decreasing the weight ratio $r$, the crystallites were found to decrease in size (Fig. 2b–e).

TEM showed that these crystalline aggregates are coexisting with vesicular assemblies (Fig. 3). Although vesicular structures (of diameters ranging from 0.5 to 2 $\mu m$) were found for all surfactant ratios, decreasing the Cremophor® A6/Cremophor® A25 ratio appears to increase the vesicle number (Fig. 3).

In the following, we will discuss a possible origin for the enhanced vesicle formation upon decreasing the Cremophor® A6/Cremophor® A25 ratio. In order to aggregate into vesicular structures, surfactants have to meet certain conditions regarding their geometrical structure [14], namely a packing parameter smaller, but close to 1 or, in other words, an HLB value around 10.

With respect to its HLB value (≈10–12), Cremophor® A6 could be regarded as meeting the conditions necessary for vesicles formation. However, at room temperature the surfactant is a wax and heating is necessary for dissolving the emulsifier. An increased temperature, in turn, causes the HLB to decrease, raising the temperature gradually weakens

![Fig. 2. Optical microscopy photographs of 1 wt.% Cremophor® A6 (a), and Cremophor® A6/A25 mixtures ($r = 9:1$ (b); $r = 8:2$ (c); $r = 7:3$ (d); $r = 6:4$ (e)) in water.](image-url)
the hydration forces between the hydrophilic moiety of non-ionic surfactants and water, reducing the water-solubility of these surfactants [15]. Consequently, at the temperature of mixing, 80°C, the HLB might be lower than 10.

In contrast, Cremophor® A25 is well water soluble, leading to clear and isotropic solutions, which can be understood by the formation of surfactant micelles. The HLB of this surfactant is higher than those of Cremophor® A6 (∼15–17). Additionally, the theoretical cloud point [16] of Cremophor® A25 lays around 165–169°C, hence well beyond the mixing temperature. As Cremophor® A25 keeps a high (even so slightly reduced) HLB value although at elevated temperatures, the addition of Cremophor® A25 might increase the HLB of the surfactant mixture to a value that allows for vesicle formation although at elevated temperatures.

3.2. Viscosity

In order to probe the interactions between the vesicular structures, viscosity measurements were performed. Samples containing concentrations ranging from 0.25 to 2.5 wt.% of a Cremophor® A6/A25 mixture with fixed weight ratio (r = 7:3) were investigated.

As shown in Fig. 4, the dynamic viscosity of the solutions shows Newtonian behaviour (η independent of the shear rate) at low surfactant concentrations and becomes progressively shear-thinning as the surfactant content increases. Already at 1 wt.% surfactant concentration, the resulting viscosity is about 10 times higher than the viscosity of water (0.93 mPa s at 23°C). Assuming a compact micellar structure the viscosity increment due to the surfactant can be estimated according to Einstein [17]. For 1.5 wt.% of surfactant this increment is expected to be about 4%. This discrepancy with the measured viscosity clearly indicates, that the surfactant solution exhibits another structure occupying a much higher hydrodynamic volume.

We have also measured the high-frequency viscosity in dependence on the surfactant concentration (Fig. 5). For disperse systems high-frequency viscosity data provide accurate access to the particle volume fraction φ. Assuming spheri-
cal particles with "hard sphere" excluded volume interaction dispersed homogeneously in a Newtonian fluid, the high-frequency viscosity $\eta'$ is related to $\phi$ according to the model of Lionberger and Russel [12]:

$$\frac{\eta'_\infty}{\mu} = 1 + \frac{3/2}{1 - \phi(1 + \phi - 0.189\phi^2)}$$

(1)

where $\eta'_\infty$ is the limiting value of the high-frequency shear viscosity (here measured at 57 kHz), $\mu$ the viscosity of the continuous phase (about 0.93 mPa s, as the viscosity of water at 23 °C), and $\phi$ is the volume fraction of the disperse phase (including water entrapped within the vesicles).

We have made use of Eq. (1) for estimating the volume fraction of the disperse phase. The obtained disperse phase volume fraction is much larger than the volume fraction of the surfactant solely; and we can define an expansion factor $\beta$ that relates the measured volume fraction $\phi_v$ with the surfactant volume fraction $\phi_s$:

$$\phi_v = \beta\phi_s$$

(2)

From the fit in Fig. 5 we obtain a $\beta$ value of about 21 ± 1, supporting the existence of vesicular structures, in good agreement with the TEM experiments (Fig. 3).

Above 1.25–1.5 wt% Cremophor® mixture, some deviations appear between theory and experiments (Fig. 5), which could be either due to a change in vesicle size depending on surfactant concentration, a distribution of vesicle size or to the occurrence of another, probably lamellar structure [18].

The obtained $\beta$ value can now be used to estimate an average vesicle radius and compare this with the radii observed in the TEM images. If we assume for simplicity that all vesicles are unilamellar and have the same size and that all emulsifier molecules are located within the vesicle shell, then $\phi_s$ can be related to the vesicle radius $R$ and shell thickness $L$ and estimated as

$$\phi_s = n \times 4\pi R^2 L$$

(3)

Introducing Eqs. (3) and (4) into Eq. (2) leads to

$$\beta = \frac{R^3}{4L}$$

(5)

The bilayer thickness may be roughly estimated. Its maximum value can be estimated by approximately two times the length of a stretched Cremophor® A25 (Ceteareth-25) molecule (17.5 nm), hence 35.0 nm. In reality, one has to take into account that water molecules are bound to the ethylene oxide chain; however, the order of magnitude should be represented correctly by this simplified model. This value is only an upper estimate, since the major part of the bilayer is made of Cremophor® A6 (Ceteareth-6) molecules, the maximum length of which is 6 nm. Consequently, a length in the order of 12 nm may be considered as more realistic.

With the $\beta$ value obtained in the present experiments and a bilayer thickness of 12 nm, we calculate a radius of 756 ± 40 nm, which is in good agreement with the observed radii range of 500–1000 nm from the TEM images. The relatively good agreement of the data with this simple model indicates that the assumption of unilamellar vesicles is reasonable, suggesting that the percentage of multilamellar vesicles is, if existing, rather small.

### 3.3. Effect of vesicles on the viscosity of an emulsion

Structure formation and viscosity of the surfactant play also an important role for the flow behaviour of complete emulsion formulations. This is demonstrated for a model emulsion of 20% paraffin oil-in-water using the Cremophor® A6A25 mixture (7:3) as surfactant. As shown in Fig. 6a, the
Fig. 6. (a) Viscosity vs. shear rate in dependence comparing the viscosity of the pure surfactant solution with those of an emulsion containing 20% paraffin oil. The dashed line shows the theoretical value for a suspension with 20% disperse phase volume fraction with hard sphere repulsive interaction. (b) Flow curves of an SDS-stabilised emulsion containing 20% paraffin oil for comparison. Independent of the surfactant concentration, the viscosity is close to the theoretical value.

Emulsion viscosity is clearly much higher than expected for a homogeneous suspension of particles/droplets with hard-sphere or even short-range repulsive interaction (dashed line in the Fig. 6a), which can be easily estimated according to the well-known Quemada equation [19]:

$$\eta = \left(1 - \frac{\phi}{\phi_{\text{max}}}\right)^{-2}$$

with $\phi_{\text{max}} = 0.61$ and $\phi = 0.2$ the emulsion viscosity $\eta$ is expected to be 2.2 mPa s.

For comparison, we have prepared similar emulsions stabilised with SDS. The viscosity of these emulsions is close to this estimated value (Fig. 6b).

The emulsion viscosity made up with 2.5% of Cremophor® A6/A25 mixture is close to that of the surfactant solution itself. Obviously, the vesicles and/or the lamellar network built up by the surfactant molecules are the dominating contribution to the viscosity of the emulsion. The somewhat lower viscosity of the emulsion is presumably due to the fact that part of the surfactant is adsorbed to the surface of the oil droplet and cannot contribute to the formation of vesicles. The emulsion viscosity increases when surfactant concentration is raised to 5%, since then more surfactant is available for vesicle formation. Further addition of surfactant leads to a drastic drop of emulsion viscosity. This is due to the change in droplet size, as given in Fig. 7 [20]. The corresponding strong increase of internal surface traps surfactant molecules, which can no longer contribute to the vesicle and/or lamellae formation. Obviously, this effect outweighs the effect of droplet size by far, since with decreasing droplet diameter, the viscosity is expected to go up, due to the increase of particle interactions and Brownian motion contribution to the viscosity. Going from 7.5 to 10% surfactant concentration results in a slight increase in viscosity, showing that again more surfactant is available for vesicle formation. Finally, the emulsion rheology can be understood in terms of multiphase system including oil droplets and large surfactant vesicles at least qualitatively.

The thickening effect of the vesicles is essential for the stability of such emulsions against creaming. The emulsion made up with Cremophor® does not exhibit any creaming within a storage time of weeks or month, while the SDS-stabilised system creams within hours.

4. Summary

In this article we have presented vesicle formation from commercial surfactant mixtures. We show how changing the composition of the surfactant mixture enhances vesicle formation by adjusting the effective HLB of the surfactant mixture. By applying the Lionberger-Russel model to high-frequency viscosity measurements we were able to estimate the hydrodynamic volume and the average size of the vesicles, which is in good agreement with the electron microscopy data. Our results demonstrate that the high-frequency viscosity data can provide a valuable indication for vesicle formation.
Finally, we present the strong impact of vesicle formation on the rheological properties of a complete oil-in-water emulsion, demonstrating a considerable thickening effect of these vesicles within the emulsion. This phenomenon is essential for the stability of the emulsions against creaming.

References