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Influence of Hydrophilic Surfactants on the W1–W2 Coalescence in Double Emulsion Systems Investigated by Single Droplet Experiments

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Abstract: Double emulsions are a promising formulation for encapsulation and targeted release in pharmaceutics, cosmetics and food. An inner water phase is dispersed in an oil phase, which is again emulsified in a second water phase. The encapsulated inner water phase can be released via diffusion or via coalescence, neither of which is desired during storage but might be intended during application. The two interfaces in a double emulsion are stabilized by a hydrophilic and a lipophilic surfactant, to prevent the coalescence of the outer and the inner emulsion, respectively. This study focuses on the influence of the hydrophilic surfactant on the release of inner water or actives encapsulated therein via coalescence of the inner water droplet with the outer O–W2 interface. Since coalescence and diffusion are difficult to distinguish in double emulsions, single-droplet experiments were used to quantify differences in the stability of inner droplets. Different lipophilic (PGPH and PEG-30 dipolyhydroxylstearate) and hydrophilic surfactants (ethoxylates, SDS and polymeric) were used and resulted in huge differences in stability. A drastic decrease in stability was found for some combinations, while other combinations resulted in inner droplets that could withstand coalescence longer. The destabilization effect of some hydrophilic surfactants depended on their concentration, but was still present at very low concentrations. A huge spread of the coalescence time for multiple determinations was observed for all formulations and the necessary statistical analysis is discussed in this work. The measured stabilities of single droplets are in good accordance with the stability of double emulsions for similar surfactant combinations found in literature. Therefore, single droplet experiments are suggested for a fast evaluation of potentially suitable surfactant combinations for future studies on double-emulsion stability.

Keywords: encapsulation; interfacial properties; controlled release; surfactant interaction; diffusion and coalescence time analyzer; DCTA; ethoxylates; SDS; PGPR

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1. Introduction

The most commonly found type of multiple emulsions is the water-in-oil-in-water (W/O/W) double emulsion. Other types, like the oil-in-water-in-oil (O/W/O) double emulsion or multiple emulsions with more than three phases exist but are not as widespread as the W/O/W double emulsion. In this case, a water-in-oil (W/O) emulsion is dispersed in a second water phase. As the inner and outer water phases typically differ in their composition, the outer phase is often referred to as W2 and the inner phase as W1, resulting in the abbreviation of W1/O/W2 double emulsion. These emulsion systems are suitable for the encapsulation of water-soluble ingredients for pharmaceuticals, cosmetics or food [1–3]. The encapsulated substance is dissolved in the W1 phase and then protected by the oil layer separating it from the outer water phase. Over time or with specific triggers like changes in pH or temperature, the encapsulated substance can be released. Another possible application would be the production of fat-reduced food emulsions [4,5]. In this case, a part of the oil in an O/W emulsion is replaced by water leading to calorie reduction of

the overall product. Despite the advantages that double emulsions can offer for various applications, only a few double-emulsion-based products are available on the market today.

Since double emulsions can be produced with classic emulsifying machines, the production itself can easily be implemented industrially [6]. The challenge is to keep the emulsions stable, despite their having two different interfaces with different curvatures. The complex structure of double emulsions allows three different coalescence mechanisms [7]. W1–W1 and O–O coalescence are similar to the coalescence in a single emulsion, where two droplets contact each other and merge. W1–W1 coalescence, does not primarily change the properties of the emulsion. However, the increase of the inner droplet size can influence the release rate via W1–W2 coalescence [8]. O–O coalescence leads to the typical emulsion breakdown known from single emulsions. The droplet size increases, which leads to creaming of the droplets and in the end to phase separation. W1–W2 coalescence only occurs in double emulsions. The encapsulated inner water phase is released through coalescence. In this case an inner water droplet gets into contact with the O-W2-interface and coalesces into the W2 phase.

To prevent all three mentioned coalescence paths, two different interfacial active compounds are needed. To stabilize the W1 droplets, at least one lipophilic surfactant is used in the oil phase. To prevent the oil droplets from coalescing, at least one hydrophilic surfactant is added to the W2 phase [9]. Both surfactant types are well described for their corresponding application in single emulsions. A transfer of their behavior to double emulsions, however, is difficult. Both interfaces in a double emulsion are linked via the same oil phase, meaning the surfactants can adsorb at both interfaces and disturb the stabilization [10–12]. As a result, double emulsions are likely to separate over time or under certain environmental conditions [13]. This can either lead to a premature release of the encapsulated W1 phase or to the coalescence of the oil droplets and thus to creaming and subsequently to the separation into a W1/O emulsion and the W2 phase.

To characterize the stability of a promising surfactant combination on the applicability in a double emulsion formulation, there are two challenges to overcome. On the one hand, the interpretation of the emulsion breakdown is difficult to attribute to specific mechanisms, since the outcome can be similar for different coalescence or diffusion paths [7,14]. On the other hand, the properties of double emulsions are not as easy to measure as with single emulsions [15]. The parameter most referred to when talking about double emulsion stability is the encapsulation efficiency. Here various approaches are suggested in the literature [15]. The direct measurement of the release of an encapsulated substance into the W2 phase is one possibility. Here, the most common technique are photometry or electro conductivity measurements [1]. The release of an encapsulated substance cannot distinguish between diffusional transport of the encapsulated substance and the release via coalescence. To evaluate the amount of encapsulated water more complex measurement techniques are applied. Approaches like differential scanning calorimetry, confocal laser scanning microscopy or pulsed field gradient nuclear magnetic resonance can give quantitative information on the amount of encapsulated water and in some cases even the internal droplet size distribution. They place high demands on the stability of the double emulsions, however. The relatively long measurement times and the mechanical and thermic stress can influence the results [15,16].

Previous studies suggested single-droplet experiments as an additional tool to evaluate the stability of formulations with more than one surfactant against coalescence [17–21]. The general idea is the simplification of a double emulsion to a measurement setup where it can be distinguished between different instability mechanisms. In these experiments a single droplet is put into contact with another droplet or with a planar interface and the time between contact and coalescence of the droplet(s) is measured [18]. The longer the droplet is stable, the more stable an emulsion with the added surfactants is expected to be [17]. A limitation to this kind of measurement setup is the timescale in which a coalescence time can be measured. When the coalescences times are too short (<1 s) the determination of the moment of contact is not accurate enough to achieve a reasonable measurement. When

the coalescence times are too long (>30 min) the necessary repetitions of the measurement become very time consuming, or there is no coalescence observed at all within a defined maximum measurement time [19,22,23]. The coalescence time increases on a logarithmic rather than on a linear scale when increasing the concentration or changing the surfactant. This leads to the necessity of choosing the surfactant concentration in a window that leads to useful coalescence times.

The general applicability of single-droplet experiments on the stability of double emulsions, as well as different approaches to the analysis and interpretation of the results are described in literature [17,18,22,23]. In this work, the stability of W1 droplets against coalescence into the W2 phase is examined for a variety of different lipophilic–hydrophilic surfactant pairs. A detailed look is taken on the analysis of the statistical spread of the coalescence times within the multiple determination on each formulation. It is known, that coalescence is a statistical process and a wide distribution of coalescence times is expected [21]. Additionally, the influence of the surfactant concentration of both surfactants on the coalescence time is discussed. Some studies found an increased release rate with higher concentrations of "aggressive surfactants" [24], an effect that could also be found in this study.

Some general hints on stable formulations found in literature were used to choose the model system described in this article. The lipophilic surfactant PGPR is the most widespread used due to its applicability in food [1]. As a second possible lipophilic surfactant, PEG-30 was chosen. For the hydrophilic surfactants, some authors suggested high molecular weight, polymeric surfactants [14,17]. Ionic and nonionic low molecular weight surfactants were used as a comparison to see whether they limited stability.

2. Materials and Methods

2.1. Materials

For the experiments ultrapure water and medium chain triglyceride (MCT), Witarix 40/60 (IOI Oleo GmbH, Hamburg, Germany) were used. MCT is an oil (triglyceride) from plant sources with fully saturated C8 and C10 fatty acids, in this case with a ratio of C8:C10 = 44:56. Compared to typical vegetable oils for food products, MCT is a relatively defined and pure oil. Therefore, effects from impurities and variation in fatty acids are kept at a minimum. In addition, the MCT oil was purified for all measurements according to the method of Dopierala et al. [25]. By the purification step, a reduced interfacial tension and a reduced stability of single droplets was observed (see Section 3.1.1).

Table 1 lists the surfactants used for this study. All surfactants were kindly provided by BASF SE (Ludwigshafen am Rhein, Germany). The abbreviations introduced here are used in the research paper for better readability. All interfacial active emulsifying agents (polymeric emulsifiers as well as small molecule surfactants) are referred to as "surfactants" regardless of their chemical structure. Surfactant concentrations are given in mass fractions (wt%) and are calculated based on the mass of the phase the surfactant is dissolved in.

Table 1. List and chemical description of surfactants used in this study.

Trade Name	Abbreviation	Chemical Description	Average Molecular Weight in g/mol
Lutensol TO8	Lutensol	C13 alcohol + 8 Ethoxylates	600
Eumulgin B2	Eumulgin	C18 alcohol + 20 Ethoxylates	1100
Disponil SDS	SDS	Sodiumdodecylsulfate	300
Pluronic PE 6800	Pluronic	Polyethylene–polypropylene glycol	8400
Dehymuls PGPH	PGPH	Polyglyceryl-2 Dipolyhydroxystearate	2100
Dehymuls LE	PEG-30	PEG30–Dipolyhydroxylstearate	5000

All surfactants used in this study are standard surfactants and suitable for producing stable O/W or W/O single emulsions with MCT. A general distinction is made between hydrophilic (Lutensol, Eumulgin, SDS and Pluronic) and lipophilic surfactants (PGPH and PEG-30), which are dissolved in the outer water phase and in the oil phase, respectively. Two nonionic, one ionic and one polymeric hydrophilic surfactant were compared. The nonionic surfactants (Lutensol and Eumulgin) and the ionic surfactant (SDS) are short chained and have a hydrophilic head group and a lipophilic tail, whereas the polymeric surfactant (Pluronic) has both hydrophilic and lipophilic groups distributed in the molecule. Lutensol and Eumulgin were both examined for a direct comparison of two chemical similar molecules with different molecular weight.

The choice of lipophilic emulsifiers for use in double emulsions is generally more limited. PGPH was chosen as a model surfactant for its very good stabilizing properties and its chemical similarity to PGPR, a very widely used surfactant in double-emulsion formulations [1]. PEG-30 was used as a comparison, for it is also a promising candidate in formulating stable double emulsions [26].

2.2. Choice of Surfactant Concentrations

The surfactant concentration in the single-droplet experiments in this work is set lower than it would be in a typical double-emulsion application. Therefore a rough approximation of the interface to volume ratio in a real double emulsion y_e e.g., [27] to the single droplet experiment y_m was done. For the single-droplet experiment the droplet interface can be neglected, since the O–W2 interface in the cuvette is much bigger, resulting in an approximate volume-to-interface ratio of

$$y_m = \frac{V_O}{A} = \frac{0.9e-6\ \mathrm{m}^3}{1e-6\ \mathrm{m}^2} = 0.9\ \mathrm{m} \tag{1}$$

For an exemplary double emulsion, the interface at the inner (W1–O) emulsion is much bigger, so the outer (O-W2) interface can be neglected. At a W1 disperse phase ratio of 0.6 and a Sauter diameter of 0.5 µm for the W1-droplets the number of inner W1-droplets n_{W1} within the volume of the oil phase V_O can be calculated the following:

$$n_{\mathrm{W1}} = \frac{\phi \times V_{WOW}}{\frac{4}{3} \times \pi \times r^3} = \frac{0.6 \times 1 \times 10^{-6}\ \mathrm{m}^3}{\frac{4}{3} \times \pi \times (0.25 \times 10^{-6}\ \mathrm{m})^3} = 9.17 \times 10^{12} \tag{2}$$

$$y_e = \frac{V_O}{A} = \frac{(1-\phi) \times V_{WOW}}{n_{W1} \times 4 \times \pi \times r^2} = \frac{0.4 \times 10^{-6}\ \mathrm{m}^3}{9.17 \times 10^{12} \times 4 \times \pi \times (0.25 \times 10^{-6}\ \mathrm{m})^2} = 5.56 \times 10^{-8}\ \mathrm{m} \tag{3}$$

$$\frac{y_m}{y_e} \approx 16 \times 10^6 \tag{4}$$

This results in a 16 million-times higher interface in an emulsion compared to available interface the single droplet experiment. As a result of this difference the surfactant concentration in single-droplet experiments is largely reduced from typical values of 1–5 wt% to 0.001–0.1 wt% in this study.

2.3. Interfacial Tension Measurements

Interfacial tensions were measured with a pendant drop tensiometer (OCA 15 LJ, DataPhysics Instruments GmbH, Filderstadt, Germany) at a constant temperature of 20 °C. The measurements were done on a 10 µL droplet, hanging from a 0.91 mm outer diameter needle. The shown interfacial tensions were obtained after an equilibration time of 60 min and measured in triplicate.

2.4. Coalescence of Single Droplets

In Figure 1, the measurement setup for the determination of the coalescence time is shown. This measurement concept was proposed by Neumann et al. [18] under the name of "Diffusion and Coalescence Time Analyzer", short DCTA.

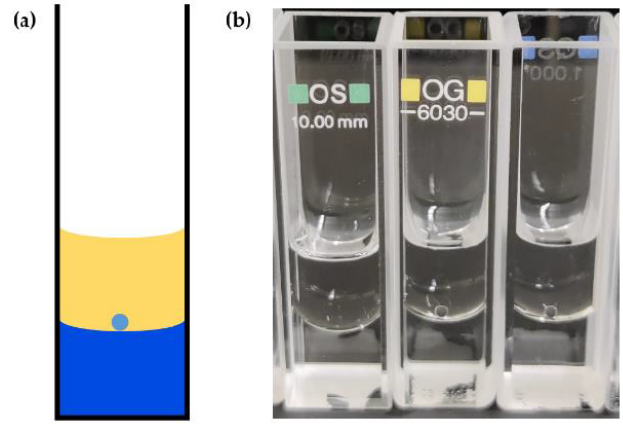


Figure 1. Measurement setup for the coalescence time measurement. (**a**) Sketch of the phases. The continuous water phase W2 (dark blue) with hydrophilic surfactant and the oil phase (yellow) with lipophilic surfactant. The W1 droplet (light blue) is without surfactant. (**b**) Photography of three measurement cuvettes. The droplet on the left is already coalesced, while the middle and the right droplet are still at the interface.

The setup has been slightly altered for this work and will be explained shortly. Glass cuvettes (1 cm × 1 cm) were cleaned in 98 wt% H_2SO_4 solution to get rid of all potential interfacial active compounds [28]. In these cuvettes, a 0.9 cm^3 oil phase is layered over 0.9 cm^3 water phase, building a slightly concave curvature of the interface. On the one hand, this curvature corresponds to the direction of curvature in double emulsions; on the other hand, this curvature allows the droplets to sediment to the lowest point and rest. Surfactants were dissolved in the water and in the oil phase before being inserted into the cuvette. The water droplets never contained any surfactants. Droplets with a volume of 2 mm^3 were formed in the oil phase using a pipette (Eppendorf Research®, 2–20 mm^3, Eppendorf, Hamburg, Germany). The pipette was retracted so that the droplet detached at the oil–air interface and slowly sank to the water–oil interface. At the moment the droplet detached from the tip of the pipette, the measurement started. The moment of detachment was optically much easier to determine than the contact between the sinking droplet and oil–water interface. This meant that the sedimentation time (about 1 s) had to be subtracted from coalescence times to get the actual stability from first contact of the interfaces. The offset did not change the overall coalescence times significantly, as they were mostly in time scales over 60 s. The measurement time ended with the complete disappearance of the droplet. After the droplet coalesced, a second droplet was added to the cuvette for a total of eight droplets in each cuvette. This measurement routine was repeated in three independent cuvettes for each measurement point, resulting in 24 coalescence times measured for each combination.

The complete process was captured with a single-lens reflex camera (EOS 700d, Canon, Tokyo, Japan) and a macro-objective (Canon EF 100 MM 1:2.8 USM, Canon, Tokyo, Japan). The interval at which images were taken during the measurement varied between 5 and 30 s depending on the stability of the system.

3. Results

3.1. General Discussion of Single-Droplet Experiments

The measurement of the coalescence times of the single droplets and the transfer of this measurement data to emulsion stabilities or the composition of an interfacial film was not carried out according to a standard method; therefore, some general limitations and possible interference factors are presented in this section.

3.1.1. Influence of the Purification Step

It is common practice to purify vegetable oils for interfacial sensitive measurements [25,28]. For this reason the oil phase was also purified before executing the coalescence time measurements, as other authors suggested [17]. The influence of oil purification on interfacial tension and coalescence time are shown in Table 2. Large differences were noted in both the interfacial tension and coalescence time. The interfacial tension was over 10% lower without the purification step. The coalescence times were enhanced by a factor of over 30 without any surfactant added to the system. This change in coalescence time was still there when additional surfactants were added (data not shown here). This showed that some interfacial active substances which did decrease the interfacial tension and stabilize the droplets, were removed by the purification and that this additional step was crucial for measuring the actual influence of the surfactants.

Table 2. Differences in the measured values for unpurified and purified oil.

	Interfacial Tension in mN/m	Median Coalescence Time in s
Unpurified oil	23.6 ± 0.8	180
Purified oil	27.0 ± 0.5	5

Although purified oil would not be used in a double-emulsion application, it seemed reasonable to work with a purified oil in this experimental setup. Firstly, the coalescence time without any surfactants added was expected to be small since emulsions without surfactants are not stable, either. Secondly, the rather high influence of the impurities in single-droplet experiments can be explained by the volume-to-interface ratios in the test and in a real emulsion, which vary hugely. In the model, there was over 16 million times more volume per interface than in a double emulsion (see Section 2.2). The amount of impurities in the oil therefore had a disproportionately large share on the result of the single-drop experiment, and a strong reduction in impurities was recommended to achieve results closer to the behavior of a real double emulsion. However, impurities could not completely be removed by this method, as seen in gas chromatography measurements (data not shown here).

3.1.2. Statistical Considerations

In Figure 2, an example of the raw data received from the single-droplet experiment is given. Each color represents one cleaned cuvette with fresh oil and water phase. In each cuvette, eight consecutive droplets were examined. It can be seen that most of the data points lie between 40 and 150 s.

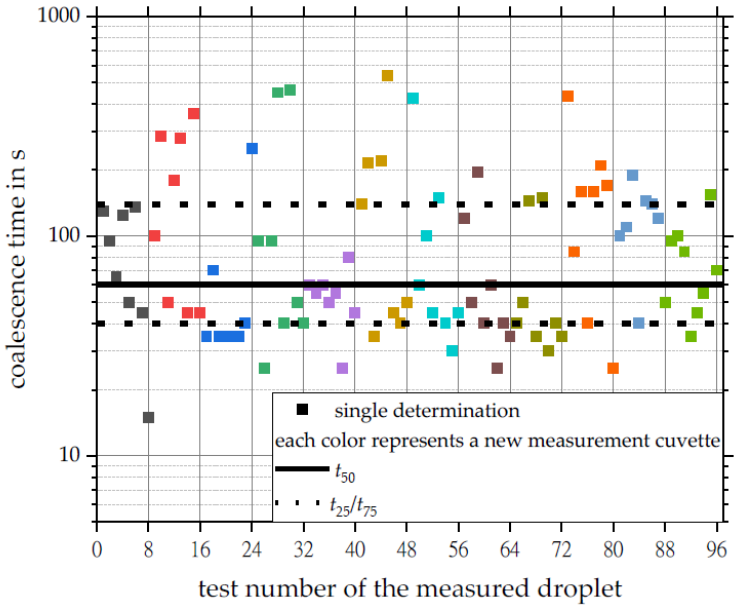


Figure 2. Repetitive measurements of single droplets with 0.1 wt% PGPH in the oil phase. Each color represents a new measurement cuvette. In each cuvette, eight droplets where measured consecutively.

The wide scattering of data points of single droplet coalescence times was reported by several authors [18,23,29–32]. The scattering can be explained by the mechanisms of film rupturing between droplets, which cannot be avoided [33]. Additionally, some coalescence times can be a lot higher than the median value, which is also found in other studies. Nevertheless these outliers are easy to distinguish from the rest of the data points and should be neglected according to Gaitzsch [21]. In conclusion, when describing the coalescence time of a certain system, there is not one value to be expected, but a coalescence time distribution.

To make sure that an influence of the selected measurement setup on the measured coalescence times was not added to the scattering, the experimental data in Figure 2 was examined on noticeable patterns. The aging of the interface over the measurement time or the disturbances of the interface by the coalescence of the preceding droplet could be excluded as an influence parameter since the number of consecutive droplets in one cuvette did not increase or decrease the coalescence time. Additionally, there was no specific cuvette in which the data points diverged from the rest, as might be the case when cuvettes are contaminated with impurities. In conclusion, the reason for the scattering of the data contributed to the underlying coalescence mechanism.

To receive reliable values from the coalescence time distribution, reference can be made to the median t_{50} and the upper (t_{75}) and the lower quartile (t_{25}). Comparing coalescence times of different formulations in Sections 3.2 and 3.3, the distributions will be plotted in boxplot form. In Figure 3, the first bar (blue) shows the boxplot of all 96 measuring points from Figure 2. The following four boxes (green) show only a quarter of the measurement points, the coalescence time of 24 droplets from three different cuvettes. Since all other surfactant combinations in this work were determined only 24 times, the influence of the statistical uncertainty on coalescence time distributions can be discussed with this figure.

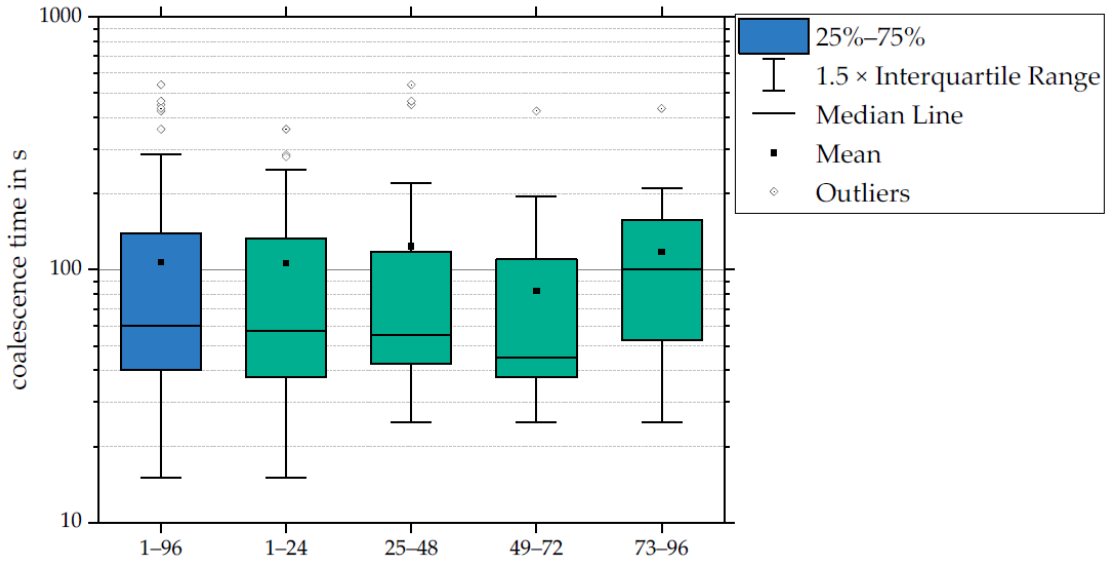


Figure 3. Data points from Figure 2 in a boxplot chart. The first boxplot shows the distribution of the complete measurement data set. The following four boxplots each show a quarter of the data. Since the variation between the four quarters is small, a 24-fold determination of each surfactant combination was deemed sufficient.

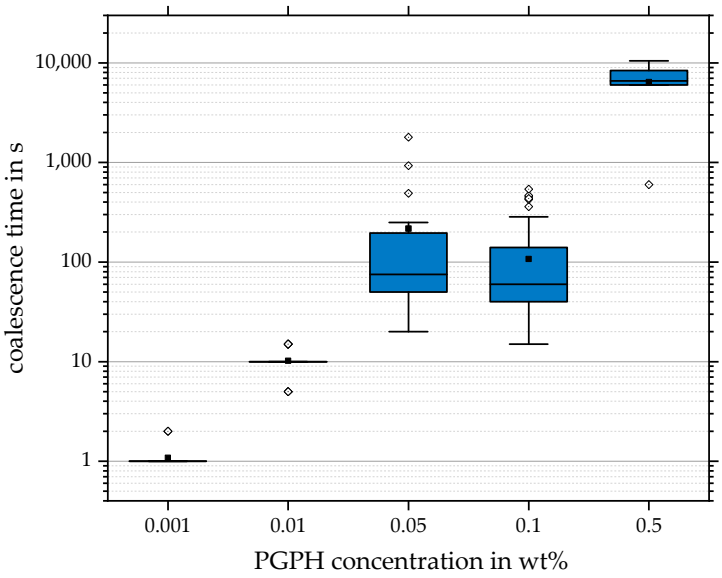
In a boxplot diagram, four key figures of the distribution can be read: The box marks the coalescence times t_{25}–t_{75} while the median value t_{50} is marked with the line within the box. Furthermore, the arithmetic mean is drawn in with the filled symbol. The whiskers show the maximum and minimum values excluding outliers, which are shown by the open symbols.

When comparing the five boxes, the first noticeable feature is that the mean value is generally higher than the median value. This is due to the fact that the outliers tend towards higher coalescence times in all evaluation groups. The median value of the four 24-fold measurement sets fluctuated between 45 and 100 s around the median of the complete measurement series, which was 70 s. Thus, a fluctuation of the median of 40% emerged from the reduction of measurements. This fluctuation can be taken as an estimation of the uncertainty of a 24-fold determination.

The number of 24 measuring points chosen for this work was a compromise between accuracy and reasonable effort for each measurement point. In summary, the following accuracy can be declared: All median values lie within the t_{25}–t_{75} interval of all other measurements. The boxes as well vary only within the range of the whiskers of the other groups. Within these boundaries, differences in coalescence times could be clearly distinguished.

3.2. Influence of the Lipophilic Surfactant Concentration

First the stability of water droplets solely with PGPH in the system had to be evaluated before the negative interactions or the synergetic effects of hydrophilic and lipophilic surfactants on droplet coalescence could be determined. The relevant data is presented in Figure 4 in a boxplot.



Interfacial tension	
PGPH in wt%	IFT in mN/m
0	27.0 ± 0.5
0.001	24.5 ± 0.9
0.01	22.2 ± 1.3
0.05	17.9 ± 0.7
0.1	12.8 ± 1.0
0.5	5.1 ± 0.4
1	3.0 ± 0.5

Figure 4. Coalescence times of water droplets with increasing amount of PGPH. The corresponding interfacial tension values are shown in the table on the right. Boxplot symbols as described in Figure 3.

The graph illustrates that the coalescence time increased with increasing PGPH concentration. It should be noted, that the coalescence times are plotted on a logarithmic scale since there is a considerable increase in stability with increasing surfactant concentration [23]. While the droplets coalesced immediately in the surfactant-free system, the most stable droplets (at 0.5 wt% PGPH) coalesced only after more than two hours. For PGPH concentrations of 1 wt% and higher, no coalescence was observed within 24 h for several examined droplets. When the coalescence times were short with low surfactant concentrations, the distribution was very narrow, caused by the applied measurement intervals. For 0.001 wt%, a photo was taken every second; for 0.01 wt% and more, every 5 s. The coalescence times for 0.05 wt% and 0.1 wt% PGPH were similar. For both concentrations, the coalescence times were around 100 s. The coalescence times with 0.05 wt% PGPH were even slightly higher. This could have been due to the remaining statistical scattering, which was discussed in Section 3.1.2.

With the increasing concentration of PGPH, the interfacial tension decreased as shown in the table right to the graph. Thus, a correlation can be drawn between the amount of surfactant at the interface and the stability of the water droplets: The higher the interfacial coverage with surfactant (low interfacial tension), the better the water droplet stability (long coalescence times).

These huge differences in coalescence time posed a limitation for the measuring technique. At a PGPH concentration of 1 wt%, no coalescence could be observed within 24 h. Therefore, a 24-fold determination, which was required for statistical reasons, was very time-consuming. Additionally, water diffusion started to influence the measurement over such long time periods that it led to changes in droplet size. This meant that the surfactant concentration in single-droplet experiments had to be adjusted in such a way that coalescence occurred between a few seconds and several minutes after droplet formation.

For the measurements of interaction between PGPH and the hydrophilic surfactants a PGPH concentration of 0.1 wt% was therefore chosen. At this concentration, there was already a significant stabilization of the water droplets observed, but still positive interactions and therefore longer coalescence times were within reasonable measurement times.

3.3. Interaction between Hydrophilic and Lipophilic Surfactants

3.3.1. Interactions between the Lipophilic Surfactant PGPH with Different Hydrophilic Surfactants

Figure 5 shows the influence of the different hydrophilic surfactants on the coalescence time of water droplets stabilized by 0.1 wt% PGPH. The hydrophilic surfactant was dissolved at a concentration of 0.1 wt% in the W2 phase. As a reference, the stability of water droplets stabilized only by PGPH and without any additional hydrophilic surfactant is shown in blue.

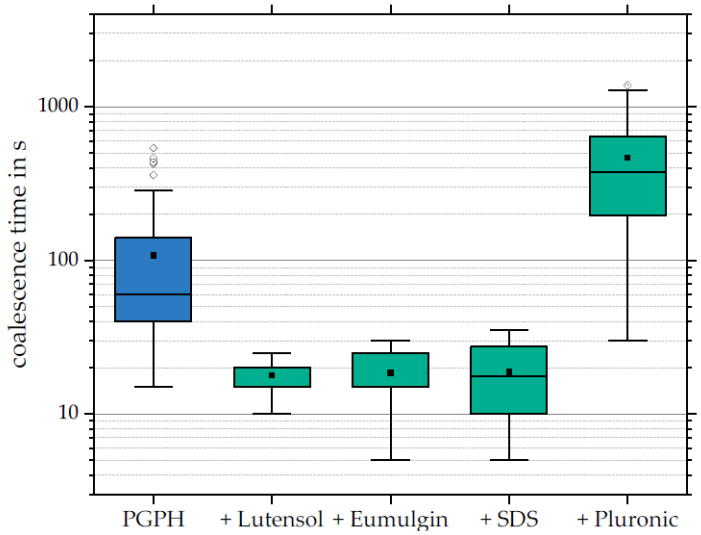


Figure 5. Coalescence time of water droplets stabilized with 0.1 wt% PGPH and additional 0.1 wt% of the four different hydrophilic surfactants. Boxplot symbols as described in Figure 3.

The addition of 0.1 wt% Lutensol, Eumulgin and SDS reduced the median coalescence time from 270 to 15 s. The destabilizing effect of the three examined hydrophilic surfactants was within the measurement accuracy the same for Lutensol, Eumulgin and SDS. In contrast, the polymeric surfactant Pluronic increased the stability of the water droplets to 400 s.

The destabilizing effect of the alcohol ethoxylates Lutensol and Eumulgin can be compared to the stabilizing properties of other alcohol ethoxylates like different types of Lutensol, Brij and Tween, as stated in the literature. When they were used in combination with PGPR, either a gelation of the W1 droplets was needed for a reasonable stability [34,35] or the stability of the double emulsion was worse than with other surfactants [36,37].

The same trends are found for SDS; however, no studies were found in combination with PGPR or PGPH. When used in high concentrations, the encapsulation results were not satisfactory with Span 80 [38,39] and PEG-30 [24] as a lipophilic surfactant.

The coalescence time of Pluronic 6800PE can be compared to other polymeric surfactants, where the advantages of a high molar mass in combination with PGPR is known in general [1,2,40,41]. Different Pluronic types also showed good encapsulation results in combination with Span 80 [42].

3.3.2. Interactions between PGPH and Hydrophilic Surfactants at Reduced Concentrations

Some studies on short chained hydrophilic surfactants mention an enhanced encapsulation efficiency with decreasing concentration of the hydrophilic surfactants [24,38,39]. Therefore, coalescence times with strongly decreased concentration of the hydrophilic surfactants were examined.

The hydrophilic surfactant was added at a concentration of only 0.001 wt% in these experiments. At this concentration, hardly any change in interfacial tension was visible in pendant-drop measurements, see Table 3.

Table 3. Interfacial tension values at a MCT–water interface interacting PGPH at 0.1 wt% with hydrophilic surfactants at different concentrations.

Surfactants	Hydrophilic Surfactant at 0.001 wt%	Hydrophilic Surfactant at 0.1 wt%
PGPH only	12.8 ± 0.1 mN/m	
PGPH-Lutensol	15.3 ± 0.7 mN/m	4.0 ± 0.4 mN/m
PGPH–Eumulgin	13.7 ± 0.2 mN/m	6.3 ± 0.1 mN/m
PGPH–SDS	13.5 ± 0.3 mN/m	10.3 ± 0.8 mN/m
PGPH–Pluronic	15.4 ± 0.4 mN/m	11.9 ± 0.2 mN/m

The addition of 0.1 wt% of a hydrophilic surfactant to 0.1 wt% PGPH decreased the interfacial tension strongly for Lutensol and Eumulgin and still significantly for SDS and Pluronic. It can be assumed that the hydrophilic emulsifiers are also located at the interface, building a mixed interface of different properties. The addition of 0.001 wt% of the hydrophilic surfactants only slightly increased the interfacial tension.

Despite the changes in interfacial tension being only small, the presence of the hydrophilic surfactant at 0.001 wt% could be seen in the coalescence times as shown in Figure 6. The overall trends are the same as with 0.1 wt% hydrophilic surfactant. Again, all short-chained surfactants reduced coalescence time and thus droplet stability, whereas the polymeric surfactant stabilized the water droplets. The destabilizing effect is less pronounced at smaller concentrations and the reduction of the coalescence time was minor here. The measured values confirmed the hypothesis found in the literature that a reduction of the hydrophilic surfactant concentration reduced the negative interactions at the interface.

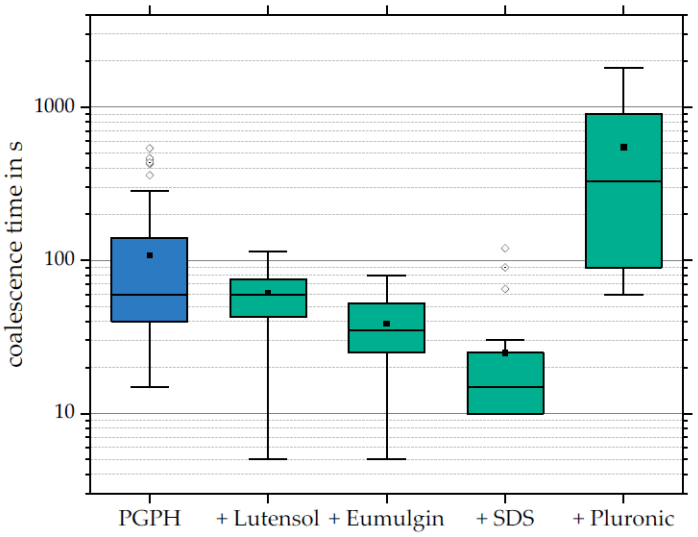


Figure 6. Coalescence time of water droplets stabilized by 0.1 wt% PGPH with additionally 0.001 wt% of hydrophilic surfactants in the W2 phase. Boxplot symbols as described in Figure 3.

Additionally, this measurement series showed the sensitivity of this measurement technique even for small amounts interfacial active impurities. The composition and thus the stability of an interface can be changed even by a small amount of hydrophilic surfactant.

3.3.3. Interactions between the Lipophilic Surfactant PEG-30 with Different Hydrophilic Surfactants

With PEG-30 a concentration row was conducted as well, and a concentration of 0.005 wt% was found suitable for the experiments with a coalescence time of 90 s. At 0.1 wt% PEG-30 the droplets did not coalesce in less than 2 h (data not shown). The hydrophilic surfactants were again added at 0.1 wt%. The results are shown in Figure 7.

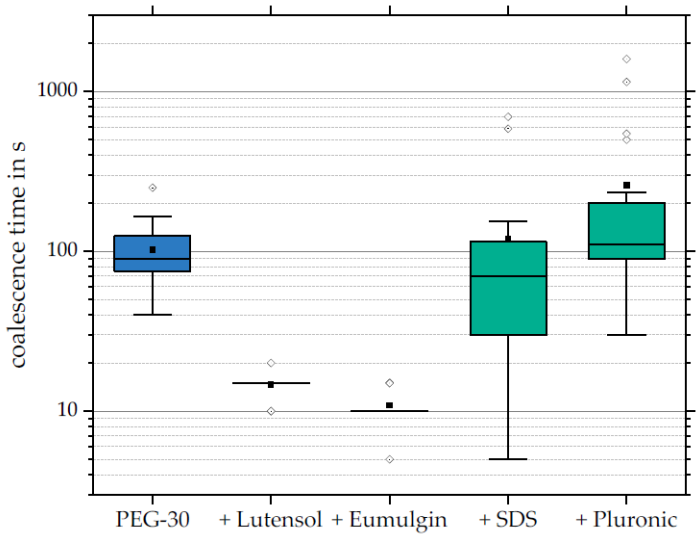


Figure 7. Coalescence time of water droplets stabilized with 0.005 wt% PEG-30 and additionally 0.1 wt% of hydrophilic surfactants in the W2 phase. Boxplot symbols as described in Figure 3.

Systems containing PEG-30 as a lipophilic surfactant behave differently to systems with PGPH. The alcohol ethoxylates Lutensol and Eumulgin still destabilized the water droplets strongly and Pluronic increased the stability slightly. The effect of SDS, however, was different. In combination with PEG-30, there was no change in coalescence time, whereas we saw a destabilizing effect in combination with PGPH.

SDS and PEG-30 also showed moderate stabilities in other studies [24]. Yafei et al. [43] produced stable double emulsions with PEG-30 and SDS and did additionally trigger the release of encapsulated substances by adding nonylphenol ethoxylates, a chemically similar surfactant to the alcohol ethoxylates used in this study. In combination with polymeric hydrophilic surfactants (proteins [44] or ethylene oxide and propylene oxide polymers [41]) good stabilities are known.

4. Discussion and Conclusions

In this study, we conducted single-droplet experiments on different surfactant combinations potentially interesting for double emulsion formulations. Our main objective was to evaluate the proposed methodology for measurement procedure and data evaluation. Subsequently, we investigated different emulsifier combinations with regard to their expected stabilizing or destabilizing effect in double emulsion applications.

With numerous repetitions of each experiment, statistically reliable data on the stability of each formulation was obtained although the coalescence times of single droplets showed rather broad distributions instead of a single value. Errors that arose due to the measurement setup were excluded, and the scattering of the values could be explained by the nature of coalescence mechanisms. Nevertheless, differences among various formulations could nevertheless be identified since the spread within one measurement series was smaller than the differences among the formulations.

To summarize, the single-droplet experiment could detect changes in the interfacial composition of surfactants even at very small concentrations and showed potential negative interactions among surfactants that can hinder the production of stable double emulsions. This experiment can be suggested as an additional tool in double-emulsion research within some limitations:

- The concentration of the surfactant in the experiment must be determined empirically since the coalescence time must on the one hand be fast enough (shorter than 2 h) to prevent changes due to aging and diffusion. On the other hand, the coalescence time must be long enough to allow the optical detection of interface contact. A direct trans-

fer of the surfactant concentration in single-droplet experiments to double-emulsion systems was not possible due to the significantly different volume-to-interface ratio.
- Experiments must be performed very carefully and with purified substances since small concentrations of interfacial active impurities can change the results significantly.
- Each experiment must be repeated several times since the coalescence time distributions measured are rather wide and must be approximated by a multiple determination.

For the examined surfactant combinations, we found tendencies that corresponded to those reported in the literature for double emulsions prepared with these emulsifier combinations. While alcohol ethoxylates like Lutensol and Eumulgin are good surfactants for O/W single emulsions, they showed negative interactions in single-droplet experiments with both examined lipophilic surfactants, PGPH and PEG-30. The stability of single droplets decreased significantly at high concentrations (0.1 wt%) but did show only small influence for reduced concentrations of 0.001 wt%. In general, it can be said, that the destabilizing properties of alcohol ethoxylate seemed to exist throughout many other lipophilic surfactants in double emulsion applications as well, for example: Span 80 or polyether-modified siloxane [39,45,46].

SDS as an exemplary ionic surfactant did reduce the stability in combination with PGPH at both concentrations, whereas it did not disturb the interface in combination with PEG-30. The polymeric surfactant examined did not show any negative interaction in all experiments and did enhance the stability with both lipophilic surfactants. Additionally, good agreement with interfacial tension measurements was found. Higher interfacial coverage at higher lipophilic surfactant concentrations was seen in both interfacial tension and coalescence time. When lipophilic and hydrophilic surfactants were combined in interfacial tension measurements, additional adsorption of the surfactant was seen, which also affected the coalescence times.

The results of this study point out the challenges in finding suitable double-emulsion formulations since the stability of single droplets could not be associated with a single parameter. Both surfactants must fit each other and the concentration of the surfactants must be chosen carefully. In further studies, single-droplet experiments can also be used to study further parameters like the influence of encapsulated substances on the coalescence time or the examination of W–W1 and O–O coalescence, the other two coalescence mechanisms influencing the stability of double emulsions.

For a deeper understanding of the mechanisms leading to destabilization of the affected interfaces by the interaction of the emulsifiers, one has to resort to complementary methods. We propose here, for example, molecular modeling. This should be experimentally complemented by analytical methods to visualize the arrangement and interactions of molecules at interfaces on a molecular level, e.g., sum frequency generation spectroscopy.

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