

The Effect of High Shear Homogenization on Physical Stability of Emulsions

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Abstract

Emulsions are thermodynamically unstable systems where droplet size is one of the main factors that affect its physical stability and consequently their quality. In this context, this work analyses the incorporation of a high shear homogenization step in the manufacturing process of an emulsion with the objective of maintaining its physical stability. In order to demonstrate the effects of this homogenization in the manufacturing process, the emulsion characterization was carried out by microscopy, rheology, laser diffraction and analytical photo-centrifugation techniques. The effect of high shear homogenization into the emulsion physical results was dependent on the speed applied to the homogenizer pump, with an effective 3600 rpm speed. There was no evidence of change on pH attributes and emulsion density, although there was a change in volumetric relationship between the droplet family presented in each sample, reducing the population of larger droplets to form a third family of intermediate droplets and increasing the volumetric proportion of the population of smaller droplets. This profile change in the droplet size distribution contributed to increased viscosity and emulsion without the presence of separation after it was submitted to the stress condition of temperature and agitation.

Keywords: emulsion, physical process, droplet size, high shear homogenization

1. Introduction

Emulsions are widely used as vehicles for cosmetic and pharmaceutical industry where various cosmetic or semi-solid pharmaceutical products are formulated as water in oil emulsion (W/O) or oil in water (O/W). Emulsions are systems with two immiscible liquids (oil and water) and may contain an emulsifying agent with the function of promoting emulsion stability due to its property of allocating in the oil and water interface decreasing the interfacial tension between these phases. Because the emulsion is considered a thermodynamically unstable system, it may present lack of long term stability.

It was reported in a publication by Raikar et al. (2011) that commonly used techniques for emulsification require the application of mechanical energy to the two immiscible phases and stabilization of the newly formed interfaces by surfactants.

Studies conducted to stabilize emulsions generally focus on the use of emulsifiers, as reported on relevant studies from Tadros (2006) and (2009) Baret et al. (2009). The use of emulsifiers in order to stabilize an emulsion certainly requires a change in the qualitative or quantitative formula of the product. There are other published works with guidance for stabilization of an emulsion, based on studying of the manufacturing process with the aim of improving the manufacturing step. Schultz et al. (2004) classify the different equipment used in the emulsion homogenization step as high pressure homogenizers, and high shear homogenizers; it is possible to observe that such equipment promotes reduction of droplet diameter, ensuring emulsion physical stability.

Established products already commercialized, have a registered formula composition, sometimes patented, where their physical stability was confirmed in the climate zone condition in the region in which this product is marketed. When there is a need to adapt the physical stability of the product already registered to address, for example, different climate zone conditions or manufacturing site changes, formula amendments will impose regulatory barriers. However, improvements in the manufacturing process steps will be a more viable alternative from a regulatory and financial perspective.

This work aims to study the additional step of high shear homogenization through a high shear homogenizer rotor-stator type pump at the end of an emulsion manufacturing process. Moreover, the ability of the high shear homogenizer to reduce the size and to increase uniformity of the droplets to maintain the emulsion physical stability was evaluated. Additionally, to prove the effectiveness of the homogenizing pump, the emulsion physical characterization was performed, in order to demonstrate uniformity of the droplet shape as confirmed by microscopy, and reduction of the droplet size as verified by laser diffraction as well as the reduction of phase separation by photo-analytical centrifugation under speed and temperature stress conditions.

2. Methods

2.1 Emulsion Preparation

Oil in water emulsion was prepared by phase inversion. Industrial lots of 1500Kg were manufactured in 2000L capacity vessel. Initially, the ingredients corresponding to the oil phase 1a (Organic phase component with oily solvent) were heated at 50°C. Subsequently, the emulsion was formed by phase inversion by adding water, phase 1b. The viscosity regulators from phase 1c were added at 50°C, under agitation and recirculation through a lobe pump (Alfa Laval[®] manufacturer). The surfactant from phase 1d was solubilized in a stainless steel container with the remaining oil phase materials from phase 1d (Organic phase component with oily solvent). Subsequently, this mixture was transferred to the vessel. The emulsion was cooled down and transferred from the vessel to a stainless steel container through a lobe pump and a high shear homogenizer rotor-stator type with three stages (IKA[®] manufacturer). Table 1 presents the formulation used for seven lots.

Table 1. Formula composition

Phase	Function
1a	Organic phase component with oily solvent
1b	Aqueous phase component
1c	Viscosity regulator component
1d	Amphoteric surfactant and Organic phase component with oily solvent

Table 2 presents a summary of the conditions applied to each test.

Table 2. Test conditions summary

Test	Manufacturing Process	Lobe pump speed (rpm)	High shear homogenizer speed (rpm)
T1a	T1 ⁽¹⁾	223	-
T1b	T1 ⁽¹⁾	223	-
T1c	T1 ⁽¹⁾	223	-
T2a	T2 ⁽²⁾	223	1800
T3a	T3 ⁽³⁾	223	3600
T3b	T3 ⁽³⁾	223	3600
T3c	T3 ⁽³⁾	223	3600

(1) Process T1 – Without high shear homogenizer.

(2) Process T2 – High shear homogenizer at 1800 rpm.

(3) Process T3 – High shear homogenizer at 3600 rpm.

2.2 Emulsion Physical Characterization

2.2.1 pH

The pH of the emulsions was determined at 25°C ± 2°C, without dilution, using a digital pH meter (Mettler Toledo[®] manufacturer, Model pH / Ion meter S220). This test was performed in duplicate 24 hours after batch manufacturing.

2.2.2 Density

The density value of the emulsions was determined by Mettler Toledo densimeter Model 40, with temperature set at 20°C. The analysis was performed in duplicate 24 hours after batch manufacturing.

2.2.3 Viscosity

The viscosity of the emulsions was measured by a Brookfield viscometer model RVDV I+, with spindle number 5, temperature at 25°C and 20 rpm agitation speed. The test was performed in duplicate 24 hours after batch manufacturing. At spindle number 5 shear rate=0.

2.2.4 Rheology

The rheology behaviour of the emulsions was analysed using a rheometer from Malvern Kinexus manufacturer, KNX5001 model. The equipment was set to apply an upward continuous shear rate from 0.01 to 1000 Pa at 25°C. The measurement was done 30 days after batch manufacturing.

2.2.5 Droplet Size

The droplet size distribution from the dispersed phase of the emulsion was evaluated by laser diffraction using the equipment Mastersizer Microplus from Malvern Instruments. The required dilution was performed with purified water to obtain obscuration from 10% to 20% in the equipment. The measurement was done 30 days after batch manufacturing. The droplet size distribution (Span) was reported in the form of cumulative percentage volume $d[v; 0,1]$, $d[v; 0,5]$, $d[v; 0,9]$ and mean droplet diameter ($d [4,3]$). The equipment also calculated the polydispersity index which is an indication of the width of the droplets, reported as range: $(d [v; 0,9] - d [v; 0,1]) / d [v; 0,5]$.

2.2.6 Microscopy

The droplet shape analysis was carried out by optical microscopy microscope Axio Imager Carl Zeiss, model M2M with DIC (interference contrast microscopy). The analysis was performed 30 days after batch manufacturing. The cover slip was gently placed in order to not break emulsion structure.

2.2.7 Analytical Photocentrifuge

In order to check the possibility of phase separation, the centrifuge was performed 24 hours and 30 days after emulsion manufacture stored at $25^{\circ}\text{C} \pm 2^{\circ}\text{C}$. For this study, centrifuge equipment, model Cientec CT-6000R was used. Centrifugation was performed at 3500 rpm for 15 minutes. From the tubes where separation was observed, the separated phase was removed and weighed to compare the amount of each separated sample.

Beyond the conventional centrifuge test, predictive assessment of physical stability of the emulsion was also carried out after 30 days of manufacture stored at $25^{\circ}\text{C} \pm 2^{\circ}\text{C}$, by checking phase separation through LUMiSizer[®] equipment. The equipment is an analytical photo-centrifuge system for measuring the intensity of light transmitted as a function of time and position along the entire length of the sample. The analysis was conducted at 45°C and rotation speed of 4000 rpm.

3. Results and Discussion

3.1 Manufacturing Process

The processes T1, T2 and T3 have in common the same manufacturing steps through the formation of the emulsion by phase inversion and differ only in the last homogenization step when the emulsion passes through a high shear pump, as summarized in the flow reported in Figure 1.

The lobe pump operating by a positive displacement (Eggert, 2011), was used in the manufacturing process with the function of recirculation in the vessel to enhance mixing of the ingredients in the formulation. Moreover, this pump was also used with the function of emulsion pumping, feeding the high shear homogenizer pump IKA[®] manufacturer at a flow of 2400 liters/hours. This flowrate was confirmed weighing the product that was transferred and time transference. The objective was to keep a steady feeding flow to the homogenizing pump. Thus, the emulsion residence time in the high shear homogenizer pump is constant for the seven tests. Keeping the residence time of emulsion in homogenizer pump, the speed of the homogenizer pump was changed for process T2 (1800 rpm) and process T3 (3600 rpm), in order to assess the effect of speed on the ability to promote different shear on the emulsion droplets. The shear rate applied in a rotor-stator homogenizer pump may increase emulsion temperature (Felton, 2013). It was also observed by Raikar et al. (2011) that substantial increases in the emulsion temperature for multiple passes occur at high pressure. Therefore, only a single pass of the emulsion through the high shear pump was performed and the initial and final temperature of the emulsion was measured using a digital thermometer. According to Table 3, it will be seen that the single pass of the emulsion by rotor-stator system does not increase the emulsion final temperature, even at the highest shear rate at 3600 rpm.

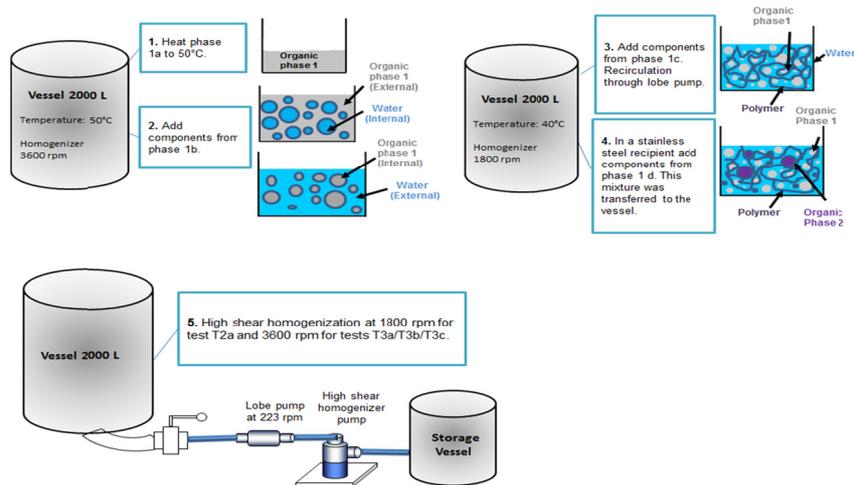


Figure 1. Process Flow

Table 3. Emulsion temperature comparison - high shear homogenizer pump step

Test	Initial temperature (°C)	Final temperature (°C)
T1a	-	-
T1b	-	-
T1c	-	-
T2a	24,8	25,3
T3a	25,1	25,3
T3b	24,9	25,1
T3c	25,0	25,3

3.2 Physical Characterization Results

The Figure 2 shows the appearance of the samples by visual inspection. There was no difference in appearance between different batches of emulsion, and all tests presented homogenous with no signs of phase separation or lumps.

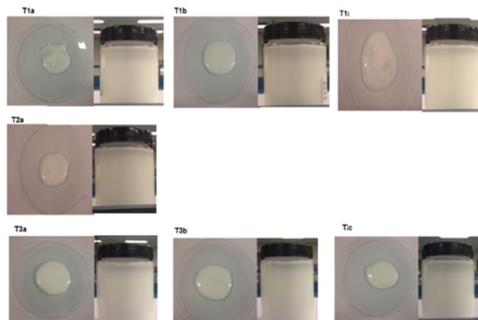


Figure 2. Samples appearance by visual inspection

3.3 pH and Density Results

There was no significant variation in the results of pH and density among different processes as observed in Table 4. It was an expected result since there was no change in the qualitative and quantitative formulation. The process difference between tests T1, T2 and T3 did not influence the ionization of the emulsion and thereby promote emulsion pH change. Regarding the density, it is possible to observe that the difference between the homogenization process does not incorporate air into the emulsion. If this had happened, a change in density result would be noticed.

Table 4. pH and density results

Test	pH	Gravity density (g/cm ³)
T1a	5,99 ± 0,03	1,0136 ± 0,0008
T1b	6,02 ± 0,03	1,0129 ± 0,0020
T1c	5,99 ± 0,02	1,0139 ± 0,0001
T2a	6,00 ± 0,03	1,0129 ± 0,0020
T3a	6,02 ± 0,03	1,0143 ± 0,0002
T3b	5,97 ± 0,01	1,0127 ± 0,0001
T3c	6,01 ± 0,02	1,0142 ± 0,0001

3.4 Droplets Size Distribution and Morphology

It can be observed in Figure 3 that the distribution of emulsion droplet size follows a bimodal model for T1 and T2 tests. It could be explained by the phenomenon of drops breakage and coalescence during emulsion formation. The breakage phenomenon leading to breakup of the dispersed phase into small droplets whereas collisions by the relative motion of the droplets lead to their coalescence forming bigger drops.

For the process T3 where the emulsions undergo high shear through a higher speed (3600 rpm), the droplet size distribution follows a trimodal model. In this trimodal distribution model, there is more than one distinct peak, describing more than one group with different droplet size ranges, with a first group of smaller droplets, a second group of intermediate droplets and the last group with larger droplets. It can be seen that all tests that do not use the final high shear homogenization step (T1) as well as the test with lower shear at 1800 rpm (T2) show a low volume of distribution peaks related to the family of smaller droplets and high distribution volume peaks related to the family of larger droplets.

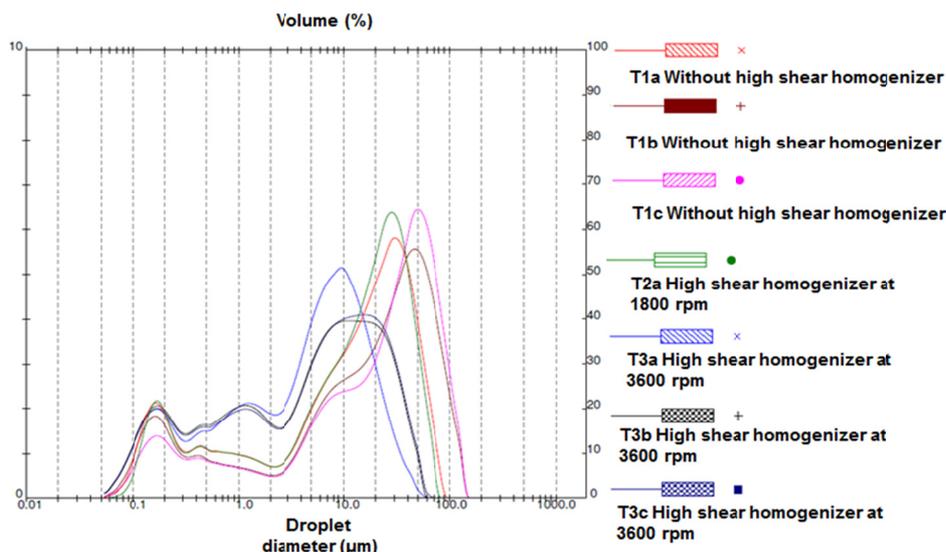


Figure 3. Droplets Size Distribution

According to Table 5, there is not a significant difference in peak distribution of smaller drops represented by d_{10} . However there is a remarkable reduction in the peak distribution for the d_{90} values for the families of larger drops, forming a third family of intermediate drops observed as d_{50} . This fact explains the increase of the Span result for T3 tests and a change in the drops distribution model from bimodal to trimodal. As reported by Paul et al. (2004) the large end of the droplets size spectrum is controlled by agitation intensity and the small end by the physics of drop breakage events. It supports the obtained result where increased intensity of the speed from high shear homogenizer increased shear which was able to reduce the large end of the droplets size. This reduction in drops distribution volume for the tests using the high shear homogenization step at 3600rpm was confirmed to be effective and reproducible for tests T3a, T3b and T3c, with noticeable difference in the outcome of size distribution $d [v; 0,9]$ reported in Table 5.

Table 5. Droplets Size Distribution

Test	$d [4,3]$ (µm)	$d [v; 0,1]$ (µm)	$d [v; 0,5]$ (µm)	$d [v; 0,9]$ (µm)	Span
T1a	18,58 18,24	0,22 0,26	13,41 13,24	45,36 44,36	3,367 3,332
T1b	29,22 29,16	0,24 0,23	20,16 19,91	72,53 71,46	3,587 3,577
T1c	32,86 29,35	0,35 0,26	25,65 21,26	77,46 75,66	3,006 3,546
T2a	17,72 17,62	0,25 0,26	13,77 13,12	41,76 42,40	3,014 3,213
T3a	7,29 7,86	0,20 0,23	4,74 5,27	18,26 19,76	3,809 3,707
T3b	9,45 9,12	0,19 0,21	5,23 5,09	26,15 24,65	4,967 4,801
T3c	9,84 9,12	0,20 0,23	5,57 5,42	26,87 25,20	4,788 4,607

The emulsion drops morphology was evaluated by optical microscopy. Figure 4 depicts the images of emulsions, showing the drops from tests T1 to be elongated, with irregular and polydispersity size. The use of the homogenizing pump at the speed of 1800 rpm in the same formulation, T2 test, gave an improvement in polydispersity of the drops, but it is still possible to observe that there is no homogeneity in this emulsion size dispersion which still presents some polydispersity. However the use of homogenizing pump at the speed of 3600 rpm in the same formulation provided a significant improvement in the shape and size of the drops, appearing more rounded.

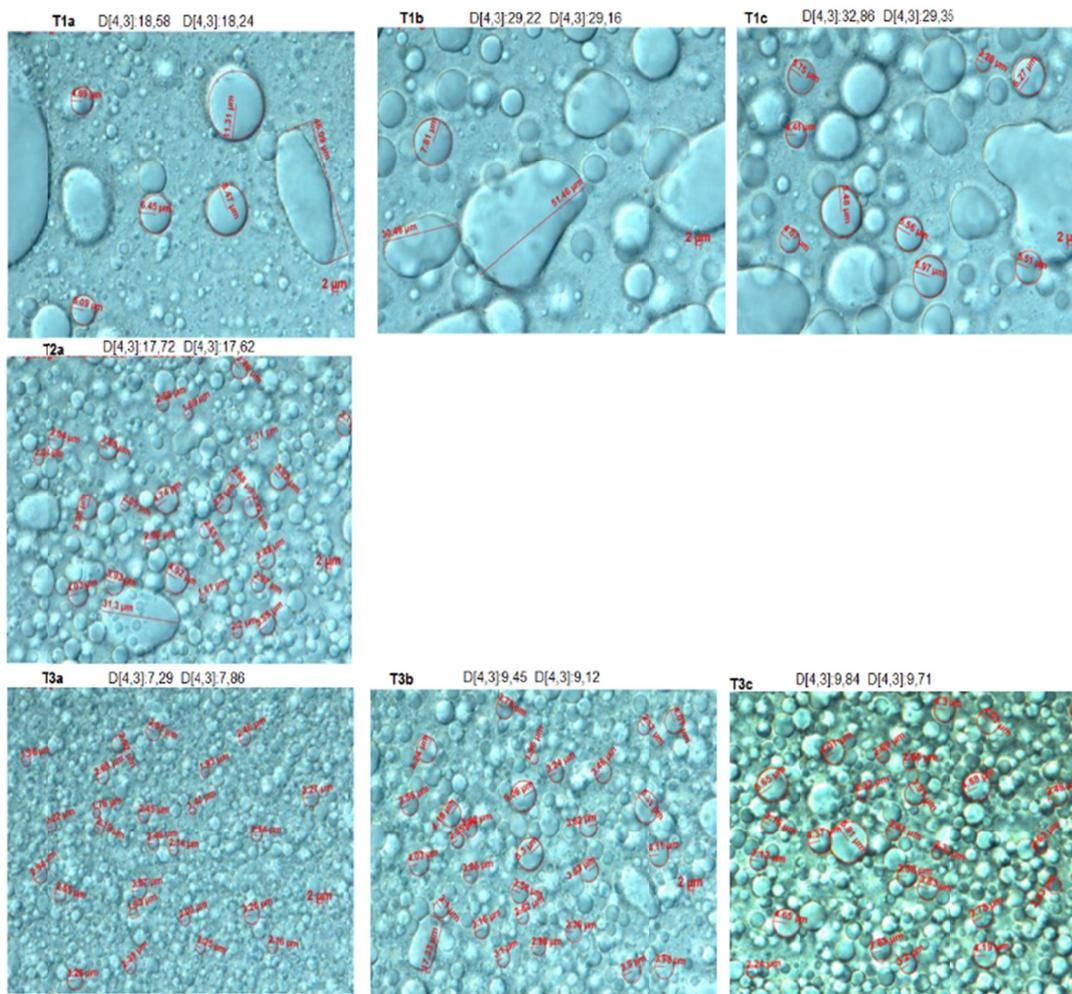


Figure 4. Samples evaluation by microscopy

Droplet images by optical microscope. 63x. D[4,3]: average diameter by laser diffraction, based on droplet volume.

3.5 Viscosity and Rheology

According to Table 6 there is an increase in viscosity in the tests that undergo high shear homogenization step (T2 and T3 tests) when compared to the T1 tests. There is an increase in viscosity of the final emulsion as the speed and shear promoted by the pump was increased.

Table 6. Viscosity results

Test	Viscosity (Pa.s)
T1a	4,009 ± 2,828
T1b	4,200 ± 1,414
T1c	4,070 ± 4,242
T2a	4,095 ± 1,414
T3a	4,290 ± 2,121
T3b	4,600 ± 0,707
T3c	4,410 ± 1,414

According to Roland et al. (2003), the increase in viscosity is associated with the decrease in drop distribution size when the agitation speed is increased during the emulsification process. Using the homogenizer pump at high speed for the T3 process increased shear emulsion, reducing the emulsion drop size and also reduced the drop polydispersity. It was also possible to observe an increase in the emulsion viscosity.

The curve from Figure 5 reports information about the rheology behaviour of the emulsion from its storage until the final use on the skin of the consumer. At the beginning of the test, the material is submitted to a very low shear rate, usually 10^{-2} s^{-1} simulating storage material. In the second stage, the material is submitted to a low shear rate of about 10^0 s^{-1} , simulating the first distribution of the emulsion, describing its flow, the facility to slide on the hands. In a third point on

the curve, the material is submitted to an intermediate shear rate (10^1 s^{-1}), simulating the action of pumping the material out of the bottle. Finally, the last stage of the test depicts the end use of the emulsion, the breaking of the sample on the hands, when viscosity decreases. It is possible to evaluate the spreadability of the emulsion on the skin. A high shear rate is applied at this stage of the test (10^2 s^{-1}).

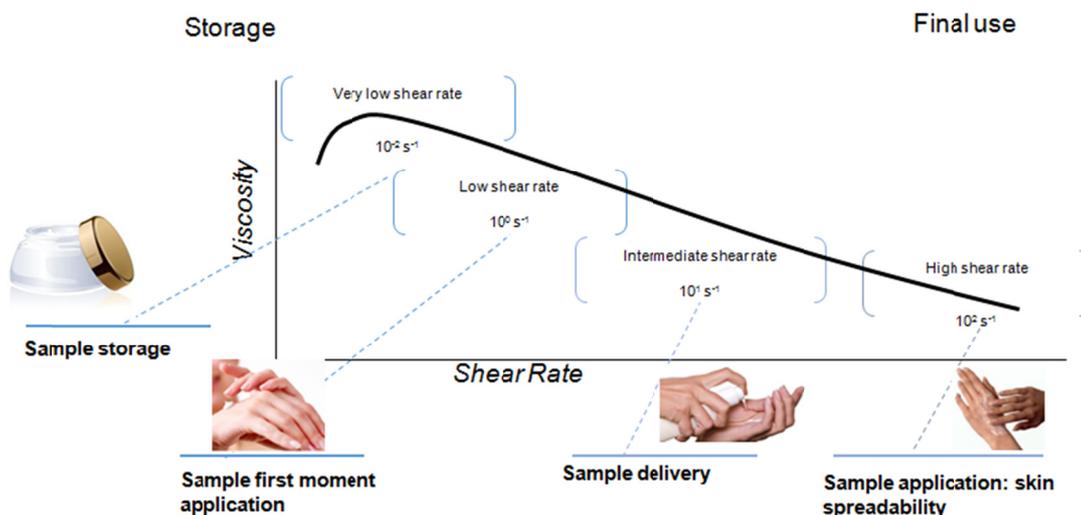


Figure 5. Rheology behaviour from storage to final use

Source: Adapted from Franck, 2001; Wood, 2001.

It is noted in Figure 6 that the application of shear produced a lower internal resistance with a consequent decrease in the apparent viscosity as the shear rate was increased, which may describe all of the batches as a non-Newtonian flow behaviour system from pseudoplastic fluid. This behaviour was expected since the formula composition has three thickening agents with pseudoplastic characteristic.

It is also observed that the use of the final high shear homogenization step in the formulations studied, although reducing the population of larger drops (noted in the size distribution of droplets), maintained the characteristics of a non-Newtonian flow curve behaviour and a pseudoplastic fluid profile for all seven tests.

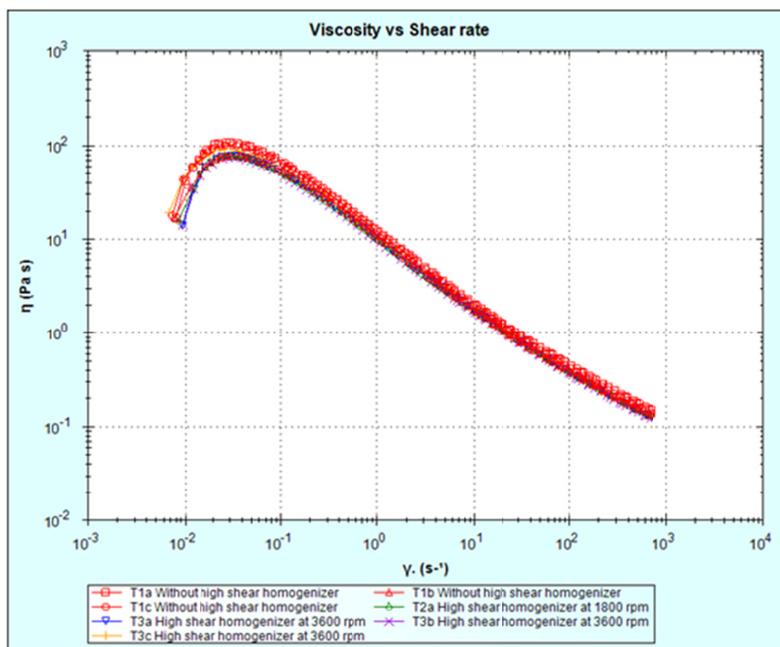


Figure 6. Comparison of viscosity versus shear rate

3.6 Analytical Photocentrifuge

It is observed in Table 7 that the factor of time (24 hours and 30 days) does not contribute significantly to an increase

or decrease in the amount of the separated emulsion expressed as a percentage. Moreover, the samples without high shear homogenisation step showed separation after centrifugation while samples with high shear homogenization step showed no separation.

Table 7. Centrifuge results comparison.

Test	Separation % - 24 hours	Separation % - 30 days
T1a	6,40 ± 0,02	6,50 ± 0,04
T1b	5,10 ± 0,02	5,10 ± 0,07
T1c	10,00 ± 0,12	10,60 ± 0,24
T2a	3,50 ± 0,01	3,54 ± 0,11
T3a	0,00 ± 0,00	0,00 ± 0,00
T3b	0,00 ± 0,00	0,00 ± 0,00
T3c	0,00 ± 0,00	0,00 ± 0,00

Additionally, the predictive assessment of physical stability of the emulsion was performed after 30 days of manufacture through LUMiSizer® equipment. In general, it can be seen from the variations of light transmission that the profiles are similar for the samples without high shear homogenization and high shear homogenization at 1800 rpm, which showed clarification at the top of the tube under stress by agitation and temperature.

This could indicate a possible phase separation due to a variation in the droplet size.

There is no overlap of the light transmission profile for these samples and it is possible to observe a displacement of the scanning light, indicating instability of the emulsion.

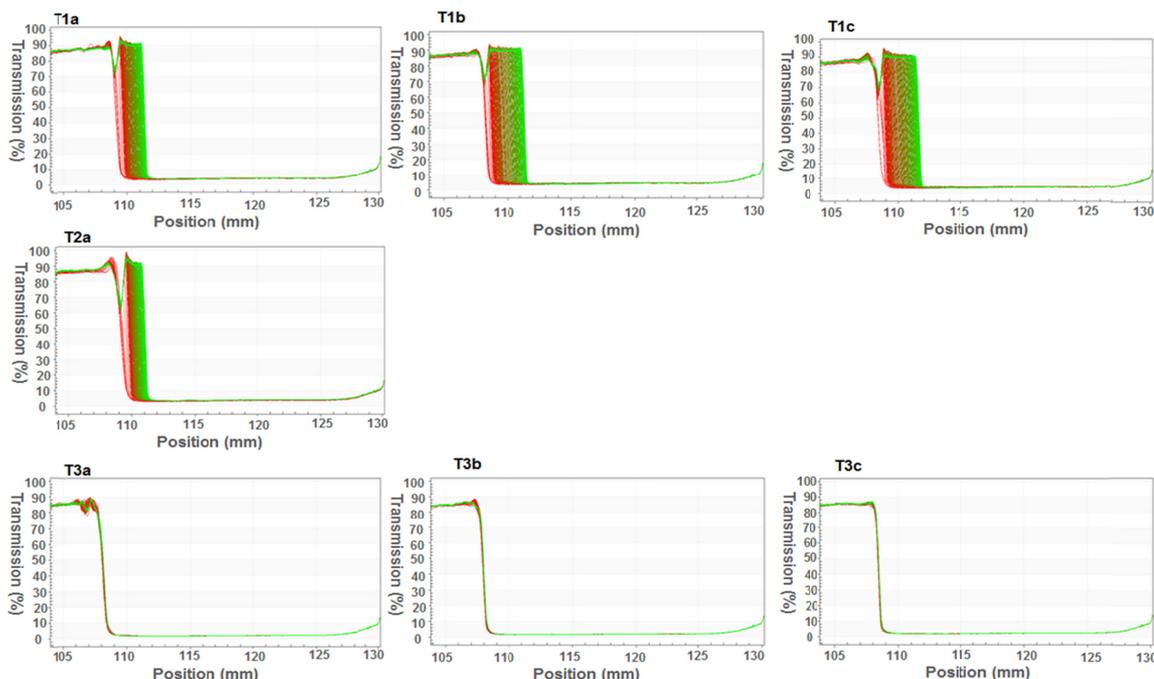


Figure 7. Transmission profile during the photocentrifuge test

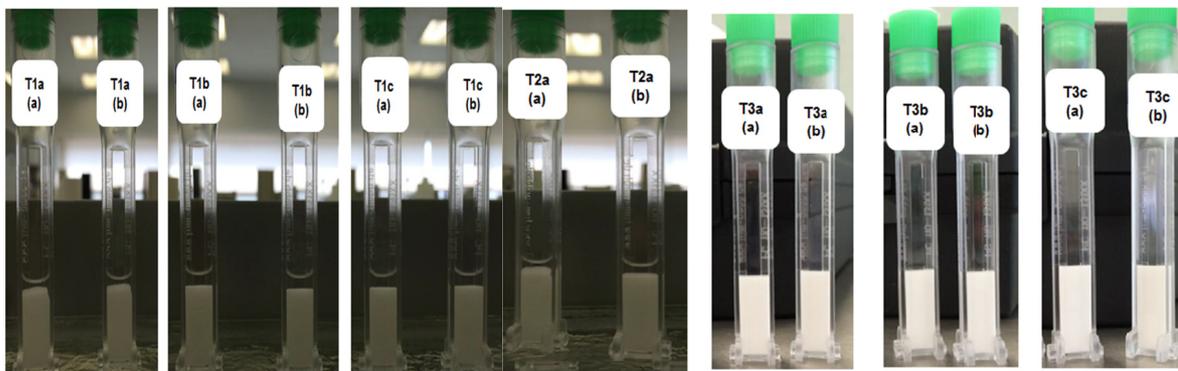


Figure 8. Visual evaluation from the tubes after the analytical photocentrifuge test: (a) First run (b) Second run

The phase separation was confirmed after the display of the tubes at the end of the analytical photocentrifuge test in LUMiSizer® equipment.

All samples without high shear homogenization step and the sample with high shear homogenization at 1800 rpm (T2a) showed phase separation at the top of the tubes, as shown in the visual assessment in Figure 8.

For the samples with high shear homogenization at 3600 rpm no phase separation was observed at the top of the tube. Those samples which passed through the high shear process had similar light transmission profile between tests T3 (Figure 7) showing overlapping of the light transmission, confirming the benefit of the additional step of high shear homogenization for emulsion physical stabilization.

Table 8 summarizes the results of the instability index and the average droplet diameter from batches studied.

It is possible to conclude that higher instability indices are obtained for samples that have a larger average droplet size, represented by $d_{[4,3]}$.

Table 8. Instability Index versus Average Droplets Sizes

Test	High shear homogenizer speed (rpm)	Instability Index	Average $d_{[4,3]}$ (μm)
T1a	-	0,2038 0,1987	18,58
T1b	-	0,2600 0,2130	29,22
T1c	-	0,2793 0,2673	32,86
T2a	1800	0,1719 0,1874	17,72
T3a	3600	0,0068 0,0052	7,29
T3b	3600	0,0074 0,0074	9,45
T3c	3600	0,0083 0,0080	9,84

The instability can be attributed to the lack of homogeneity of size and shape of the droplets present in this emulsion, as evaluated by microscopy and laser diffraction techniques. From this study, we can see that besides the presence of the emulsifier, it is also necessary to have an effective emulsification process producing a homogeneous emulsion in the shape and size distribution of their droplets.

The same qualitative and quantitative formula with the same emulsifier system gives distinct phase separation results according to the homogenization process adopted.

Using the homogenizer pump at high speed (3600 rpm) a higher emulsion shear was obtained, and consequently, there was a possible increase in the interfacial area with better distribution of the emulsifying agent around the emulsion droplets without any change in the quantities used in the formulation.

4. Conclusions

This work focused on studying the influence of high shear homogenization process in maintaining the physical stability of an oil-in-water emulsion, having the same qualitative and quantitative formula composition.

The effect of high shear homogenization on the physical properties of the oil in water emulsion was dependent on the speed applied to the homogenizer pump where 3600rpm speed was confirmed to be effective in improving the physical aspects of size emulsion, drop shape, and eliminating separation of phases when submitted to stress conditions of temperature and agitation.

There was higher emulsion shearing using the homogenizer pump at high speed allowing a better emulsifying agent distribution in the emulsion probably by the increase in interfacial area.

The benefit of high shear homogenization at the end of the manufacturing step was confirmed, due to modification of the volume ratio between the families of droplets sizes present in each sample, thereby reducing the population of larger drops, and forming a third family of intermediate drops and increasing the population of smaller droplets. This effect was also observed in optical microscopy where there was drop polydispersity reduction for the tests that used the homogenization at 3600 rpm, resulting in a slight increase in the emulsion viscosity.

The rheology behaviour showed similar yield stress and consistency index results for the samples that passed through the high shear pump, which differs from the sample without the high shear homogenization step. This difference indicates that

the samples that passed through the pump required a lower rate to start to flow, indicating a possible benefit to the consumer, due to potentially improved spreading properties of this emulsion on the skin for samples that passed through high shear homogenization process.

The high shear homogenization step proved to be feasible in maintaining physical stability of emulsions and can be an alternative to be utilized by companies in cases where a formula composition change imposes regulatory barriers.

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