TURBISCAN DNS

Online Emulsification Studies
Formulation process optimization

INTRODUCTION

Setting up the right process for emulsification requires high level of expertise to select the right tools (mixing blades & homogenization type), parameters (speed and time...). Efficiency of the processes is usually studied by particle size measurement using size analyzers set externally to the whole process. This requires tedious back and forth sampling and preparation for the instrument, limiting the analysis of full kinetics. Turbiscan®, the leading technology in direct stability measurement, provides a fast and pragmatic approach for such measurement thanks to the circulation function TLOOP.

ONLINE **NO DILUTION** **FAST**

HOW IT WORKS

Turbiscan technology, based on Static Multiple light scattering (SMLS), consists on illuminating a samplewith an infrared light s ource and acquiring backscattered (BS) and Transmitted (T) signals.

BS and T = f(φ, d, np, nf)

The signal is directly linked to the particle's concentration (φ) and size ( ) according to the Mie Theory, with refractive index of continuous ( ) and dispersed phase ( ) being fixed parameters. The measurement of the BS and T can be performed either on scanning mode, to provide homogeneity and stability measurement, or with very high frequency for fast time resolved and online measurement.

The measurements are done without any dilution & on native sample.

Additionally, the Turbiscan DNS associates 2 functions for online characterization of the dispersion state and the dispersibility :

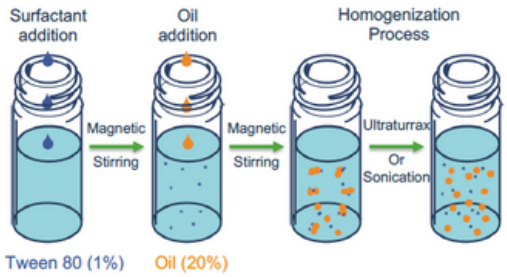
- Mixing function (TMIX) for automated fast formulation screening with a stirring bar directly inside the measurement cell. (see Notes TDNS 1-3).
- Circulation function (TLOOP) for online measurements and scale up or process optimizations. **Topic of this note.**

EXPERIMENT AND METHOD SET UP

The aim of the work: Study of the efficiency of two different homogenization methods: Sonication (US) and industrial disperser (Utraturrax - UT)

The emulsion type: 20% O/W emulsion stabilized with 1% tween 80.

Sample preparation: Surfactant is mixed with water. The oil is added to the water/surfactant solution under magnetic stirring for 2 min to create a premix. The pre-mix is homogenized at different amplitudes
and speeds for 15 minutes:



Sample analysis: The measurement of the BS and T is directly during the homogenization using **TLOOP function**: The emulsion is pumped in and out the Turbiscan cell thanks to a peristatic pump, creating a circulation loop with the formulation "reactor".

This online setup gives a direct access to a determination of native particle size under mixing. No sampling is required, and the data can be acquired up to 10 times per second. This ensures a real monitoring of the particle size evolution (droplet size, particle reduction) without any dilution nor external forces.

RESULTS

The graph 1 below illustrates the evolution of the mean particle size (dSMLS) as a function of time for the different processes and power/speed studied.

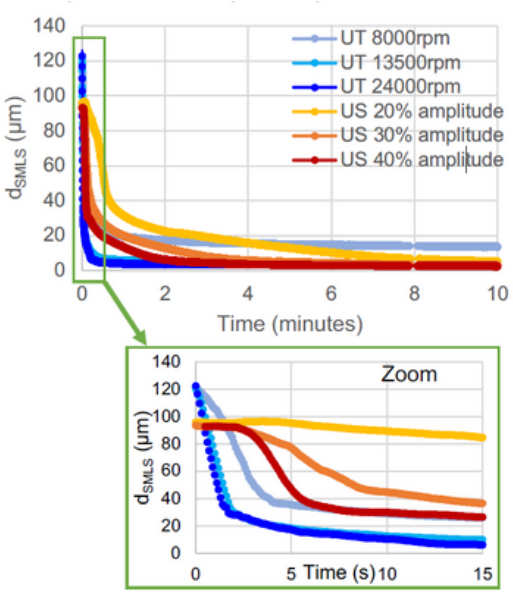


Figure 1. Emulsions particle size in function of process time

Ultraturrax versus Ultrasound

The droplet size kinetics are drastically different upon the homogenization process. In the first minutes, Ultraturrax is more efficient and reaches smaller droplet sizes. However, in the long run its efficiency drops and ultimately, it's with the ultrasound that smaller droplets are created.

Droplet size is followed from several hundred to few µm with the exact same set up, without any dilution and at high frequency for a direct and native particle size determination.

Impact of the energy

From the graph on figure 1, the final droplet size can be evaluated in function of the energy deployed. The figure 2 displays the final particle size after 10 minutes

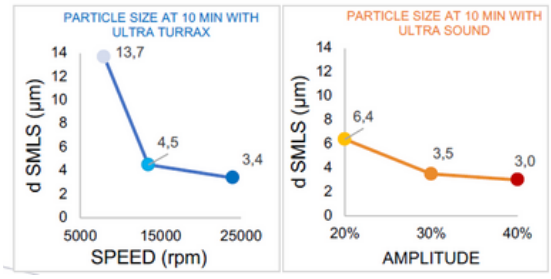


Figure 2. Particle size after 10 minutes of emulsification with ultrasound and ultraturrax

The figure 2 provides another level of understanding of the process:

- Globally, Ultrasound generates a finer emulsion smaller droplet size)
- For UT, there is a real interest to work at speed >15 000rpm to reach micron size range. However the benefit of much higher speed can be discussed.
- For ultrasound, the impact of the energy on the final droplet size is not so obvious despite a wide range of energy. The extra energy provided actually helps to speed up the size reduction process.

CONCLUSION

Turbiscan® technology associated with the TLOOP funciton offers unique screening possibilities for fast and online studies of the efficiency of the process and emulsification methods. The advantage of using Turbiscan and TLOOP module for emulsification process screening

Save time

Monitor size online during emulsification without manual sampling. The module connects directly to the formulation "reactor". As such, the time needed to sample and prepare the measurement with traditional particle size analyzers are avoided.

No dilution and on native sample

While other techniques require a high level of dilutions or additional forces and their impact is not negligible on particle size.
The Turbiscan technology offers direct measurement of the mean particle size in the native sample, as is.

All in one

Once the process is selected to achieve the desired particle size in the set time, the Turbiscan technology can also help in adjusting formulation properties and stability over time.