



# Characterization of Pickering emulsions

## - Physical stability evaluation -

PHARMACEUTICAL

### Introduction

The use of pickering emulsions is of high interest for applications in a large range of fields like drug delivery, vesicle and responsive materials, porous materials, catalytic facilitation, safer formulation in cosmetic, due to their strong stability compared to systems stabilized by surfactants. They also provide many beneficial properties: less irritability, environmentally friendly behaviour, carbon foot print decrease.

This note will present the results of a study of such emulsions on an example of pickering emulsions used in pharmaceutical field with an antifungal medication stabilized with biocompatible component. In pharmaceutical field, surfactant free emulsions are of great interest to avoid skin irritation, hemolysis and protein denaturation.

### KEY BENEFITS

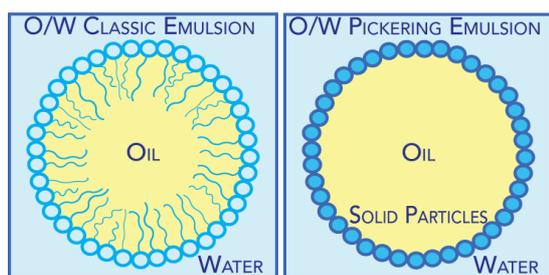
FAST  
NO DILUTION  
SENSITIVE

### Reference

L. Leclercq, V. Nardello-Rataj, *Pickering emulsions based on cyclodextrins : A smart solution for antifungal azole derivatives topical delivery. European Journal of Pharmaceutical Sciences 82 (2016) 126-137*

### Definition

A Pickering emulsion is an emulsion that is stabilized by solid particles (in the range 50-500nm) which adsorb onto the interface between the two phases.



The emulsion properties can be tuned in function of the particle affinity with water.

Particles show irreversible adsorption, in contrast to surfactant molecules, which exist in a dynamic equilibrium at the oil water interface and can adsorb and desorb on a rapid timescale. This strong adsorption of particles at the interface may also explain their stability over extended periods of time (even with large droplet sizes).

Therefore, pickering emulsions are extremely stable against destabilization phenomena such as

coalescence and Ostwald ripening and the potential to enhance oxidative stability compared to systems stabilized by surfactants. But several authors reported aggregation or flocculation when diluting samples for example for oil droplet size by laser diffraction (C. Linke, S. Drusch, *Pickering emulsions in food – opportunities and limitations. Critical reviews in food science and nutrition 58(12) (2018) 1971-1985*).

### Reminder on the technique

Turbiscan® technology, based on Static Multiple Light Scattering, consists on sending a light source (880 nm) on a sample and acquiring backscattered (BS) and transmitted (T) signal all over the height of a sample in its native state.

By repeating this measurement over time at adapted frequency, the instrument enables to monitor physical stability of a sample without dilution.

The signal is directly linked to the particle concentration ( $\varphi$ ) and size ( $d$ ) according to the Mie theory knowing refractive index of continuous ( $n_f$ ) and dispersed phase ( $n_p$ ):  $BS = f(\varphi, d, n_p, n_f)$ .

### Method : Pharmaceutical application

The most commonly used pickering particles are silica, clays, calcium carbonate, titanium oxide or latex. This study focuses on biocompatible native cyclodextrins (CD) for antifungal medication based on econazole nitrate salt to treat superficial skin infections.

Different formulations have been tested changing the oil phase and type of the cyclodextrin as listed in the table below.

| Formulation | Stabilizer | Oil                 |
|-------------|------------|---------------------|
| F1          | α-CD       | Liquid paraffin     |
| F2          | β-CD       |                     |
| F3          | γ-CD       |                     |
| F4          | α-CD       | Isopropyl myristate |
| F5          | β-CD       |                     |
| F6          | γ-CD       |                     |

Table 1 : Composition of 6 formulations of fungal Pickering emulsion

## Results

The following graphs on Figure 1 display the delta-backscattering signal for the emulsions F1 and F4 versus the sample height in function of time, from the blue to the red curves.

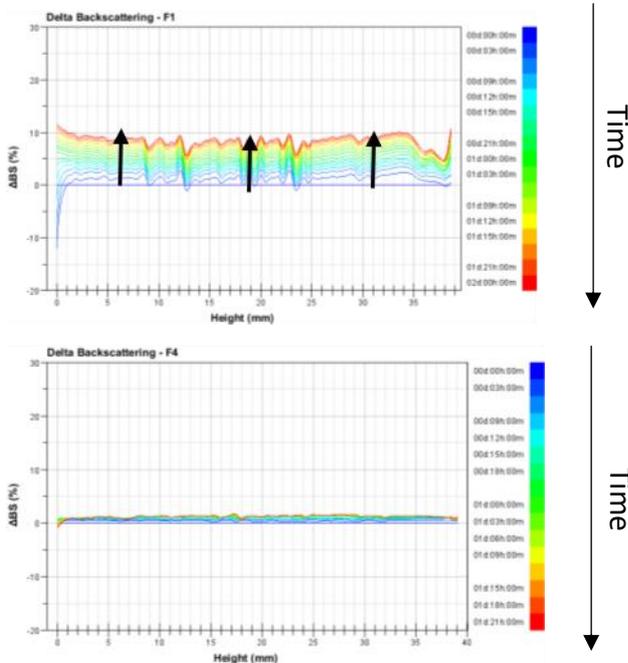


Figure 1: Backscattering evolution versus time and sample height of Pickering emulsion F1 and F4 analyzed at 25°C

The Turbiscan profiles for all samples display an evolution over the whole height of the sample meaning that the droplet size is increasing. The intensity of the variations is different from one sample to another. In other words, coalescence occurs with different intensities in the samples.

It is possible to monitor the destabilization kinetics in the samples and quantify it, thanks to the Turbiscan Stability Index (TSI). It is calculated by adding all the variations of signal detected due to destabilization phenomena (sedimentation, clarification, size variation, ...). At a given ageing time, the higher is the TSI, the shorter the stability of the sample.

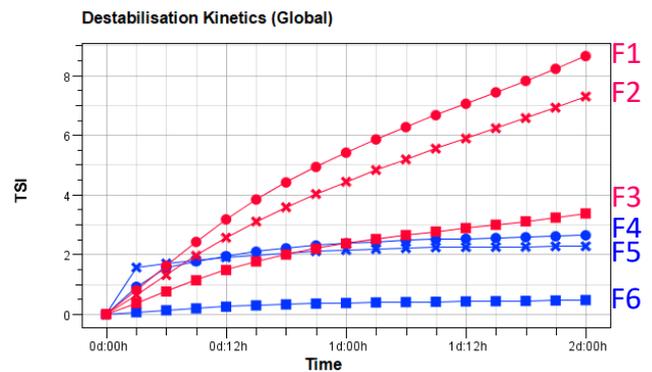


Figure 2. TSI evolution versus time and Bar chart after 2 days of analysis of Pickering emulsions F1-F6

The results allow to rank the formulations in term of stability: emulsions **F4-F6** containing isopropyl myristate oil are more stable than **F1-F3** (paraffin oil). Indeed, isopropyl myristate can establish O-H ...O hydrogen bonds with CD cavity to get higher binding constants than with myristate.

Comparing the effect of CD particles shows that emulsion with γ-CD is more stable than ones with β-CD and α-CD probably because the inclusion complex based on γ-CD is bigger and enables to bind complexes together for a more densely coating.

## CONCLUSION

Turbiscan® experiments have been performed to quantify and compare the emulsion stability of different formulations by varying the size of the cyclodextrin and the continuous phase. The coalescence is limited by the surface coating of oil/cyclodextrins inclusion complexes, without need of adding polymers or charges. And, the global physical stability ranking is realized in one-click and the interface coverage by particles is deduced from these measurements at rest and without dilution.