EFFECT OF AN ANTIBIOTIC ON THE STABILITY OF INJECTABLE EMULSION

INTRODUCTION

Lipid emulsions are commonly used to insure the delivery of antibiotics or liposoluble drugs in vaccine. These Injectable lipid emulsions are generally made with:

- Purified natural oil (soya, sesame, olive, cod-liver oil etc.)
- Aqueous phase
- Emulsifiers (natural e.g soya lecithins or synthetic e.g glycerol monostearate)

They must stay stable during the duration of use of the emulsions and the diameter of the particles/droplets must be inferior to 5µm in order to void the risk of embolism. The addition of active to the emulsion affects their properties and so all combination has to be control.

In this note, the effect of an antibiotic on 4 different lipid emulsions is evaluated.

PRINCIPLE

Measurement with Turbiscan®

Turbiscan™ instrument, based on Static Multiple Light Scattering, consists in sending a light source (880 nm) on a sample and acquiring backscattered and transmitted signal. Combining both detectors (BS & T) enables to reach wider concentration range. The backward reflected light comes from multiple scattering as the photons scatter several times on different particles (or drop).

This signal intensity is directly linked to the diameter (d), according to the Mie theory:

$$d = f(BS, \varphi, n_p, n_f)$$

More information

METHOD

Two series of samples were prepared with 4 injectable emulsions (at 10% in soya oil) from different suppliers (A, B, C and D):

- One series with serum,
- One series with an antibiotic (amphotericin (1%))

RESULTS

To evaluate the impact of the antibiotic on the emulsion stability, 3 different parameters are measured:

- Droplets migration rate
- Droplets size
- The global stability (TSI)

1- Migration rate of the droplets

In Figure 1 & 2, we can observe the variation of the intensity of the light (Y axis) versus the height of the sample. Due to the migration of the oil droplets toward the top of the sample, we can observe in both figures, an increase of the intensity of the light at the top of the sample (increase of the concentration of oil).

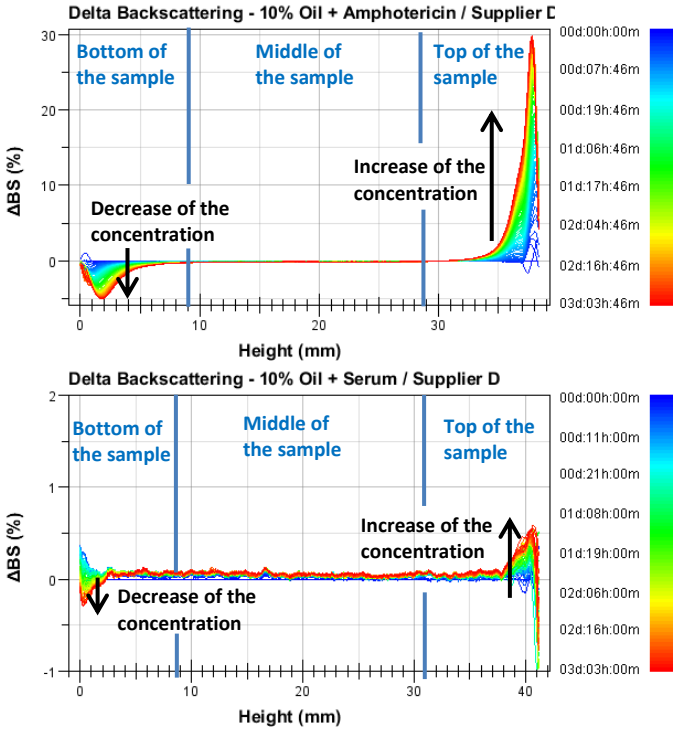

Figure 1 & 2: Variation of backscattering versus sample height for sample D with Antibiotic (top) and without (bottom)

2- Migration rate of the droplets

By measuring the thickness of the cream layer over the duration of the measurement (Figure 1 & 2), the migration rate of the oil is computed (Figure 3 & Table 1)

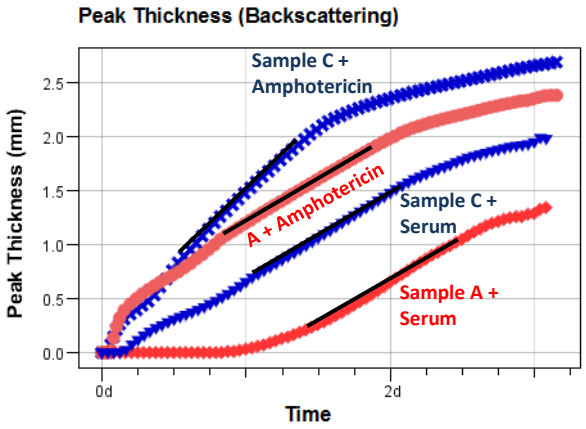

Figure 3: Peak thickness of the cream layer at the top

Supplier	Migration rate (mm/d)	
	Serum	Amphotericin
A	0.74	0.83
B	0.24	0.16
C	0.76	1.11
D	1.02	1.43

Table 1: Migration rate of the oil droplets

The addition of the antibiotic increase the destabilization kinetics for samples A, C and D whereas there in no major change for sample B.

3- Particles Size

The Turbiscan technology allows us to measure the mean diameter of the droplets in a concentrated media. Using the Mie theory law and the parameters below, the mean diameter is automatically measured from the % of backscattering at time 0.

- Refractive index of Soya oil = 1.474
- Refractive index of water = 1.33
- Volume fraction of the dispersed phase ϕ = 10 %

Supplier	Mean diameter (nm)	
	Serum	Amphotericin
A	130	130
B	190	210
C	160	170
D	215	235

Table 2: Mean diameter of oil droplets

In order to be in conformity with the specification, the mean diameter must be inferior to 400nm without dilution of the sample. Thanks to the multiple light scattering measurement, no dilution of the sample is needed. We can observe that all formulation meet the specification and the addition of the antibiotic does not impact the mean diameter.

4- Global stability

It is possible to monitor the destabilization kinetics in the samples versus ageing time, thanks to the **T**urbiscan **S**tability **I**ndex (TSI). It sums all the variations detected in the sample (creaming, size variation, …). At a given ageing time, the higher is the TSI, the worse is the stability of the sample.

Supplier	TSI (3 days)	
	Serum	Amphotericin
A	1	2.4
B	0.2	0.4
C	1.3	2.9
D	1.7	3.8

Table 3: TSI values after 3 days of measurement

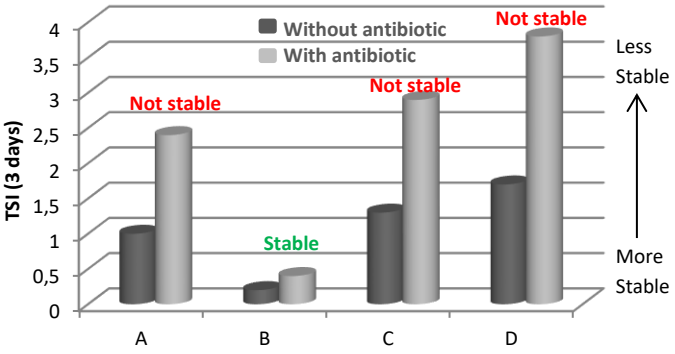

Figure 4: Impact of the antibiotic on the stability

Thanks to graph in figure 4, the impact of the antibiotic on the emulsion stability can be observed. Only the solution from supplier B stays stable even with the antibiotic.

SUMMARY

This application note shows a quick and simple method to validate the stability of injectable emulsions with antibiotics. In only 3 days of measurement, stability can be predicted. The migration rate of the droplets, the mean diameter and the global stability were compared with only one measurement per sample using the Turbiscan technology. For this specific antibiotic, it is recommended to use the injectable emulsion from the supplier B.