PARENTERAL EMULSION STABILITY

IMPACT OF ELECTROLYTES

Introduction

Lipid injectable emulsions for therapeutic nutrition must cover all the individual needs and are an essential source of fatty acids, as well as a daily source of calories. Therapeutic nutrition can be done with successive or simultaneous administration of lipid emulsion, electrolytes, and minerals. The simultaneous administration of a dispersion containing all the nutrients requires the validation of the compatibility between the nutritive elements and the stability of the lipid emulsion in the dispersion. These emulsions have been used in the clinical setting for almost 50 years, but despite this, there are no established official standards governing pharmaceutical quality. The stability of a lipid emulsion with different concentrations of calcium chloride ($CaCl_2$) was evaluated using the TURBISCAN technology.

Principle

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

Method

Emulsions of lipid emulsion were prepared by dilution of an injectable emulsion (at 10% in soy oil) and a solution of calcium chloride at different concentrations:

- Injectable emulsion (10% in soya oil)
- Calcium chloride in water at 0; 4 and 6 mMol
- Dilution ratio: 1/1 in volume

Emulsions were analyzed using the TURBISCAN technology by scanning the sample every 10 minutes for a duration of 4 hours.

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Results

By scanning the 3 samples according to the method described in the previous paragraph, the following results are obtained:

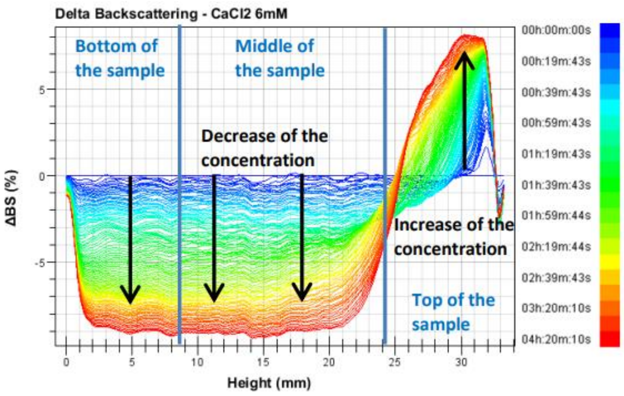

Figure 1. Backscattering variation versus sample height for a concentration of $CaCl_2$ at 6 mMol

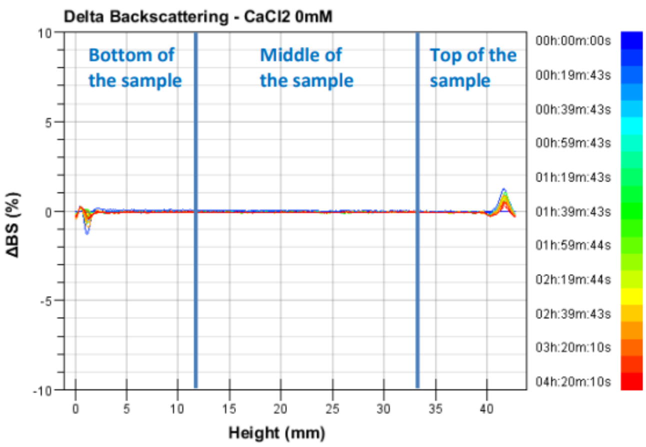

Figure 2. Backscattering variation versus sample height for a concentration of $CaCl_2$ at 0 mMol

From the graphs in Figures 1 & 2, we can observe the effect of adding an electrolyte on the emulsion stability. In Figure 2 where there is no calcium chloride, no or minor destabilization is observed whereas we can observe the following destabilization when the calcium chloride is added:

- At the top of the sample, an increase in the intensity of backscattering due to the creaming of the oil droplets and so an increase of the concentration.
- Consequently, a decrease in the signal is observed over the rest of the sample due to the decrease in the oil concentration.

To evaluate the impact of the concentration of electrolyte on the suspension stability, 2 different parameters are measured:

- The global stability (TSI)
- The creaming rate

1-Global stability (TSI)

It is possible to monitor the destabilization kinetics in the samples versus aging time, thanks to the Turbiscan Stability Index (TSI). It sums all the variations detected in the sample (creaming, clarification, size variation, …). At a given aging time, the higher the TSI, the worse the stability of the sample

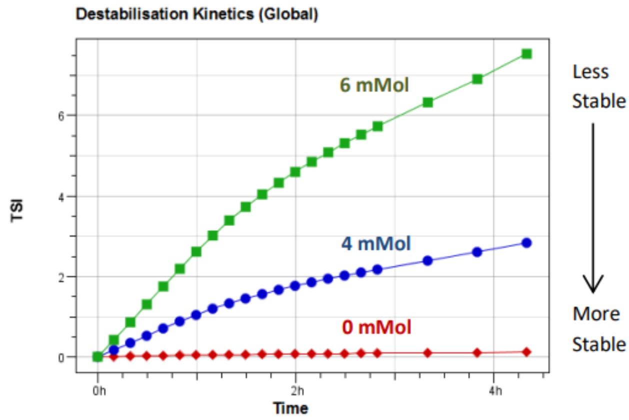

Figure 3. Turbiscan Stability Index (TSI) for all samples

Concentration $CaCl_2$ (mMol)	TSI (4 hours)
0	0.1
4	2.7
6	7.1

Table 1. TSI values after 4 hours of measurements

From Figure 3 and Table 1, we can compare the effect of the electrolyte concentration on the global stability of the dispersion. The higher the concentration of electrolyte, the more stable the sample and so the sample with 6 mMol of $CaCl_2$ is the less stable. We can observe that after only one hour we can discriminate the samples and so the duration of measurement can be adjusted for further study

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2-Creaming rate of the oil droplets

By measuring the thickness of the creaming layer throughout the measurement (Figures 1 & 2), the migration rate of the oil droplets is computed (Table 2).

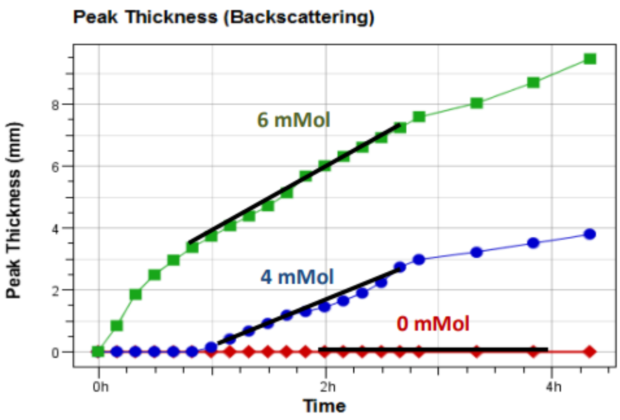


Figure 4. Peak thickness of the cream layer over time

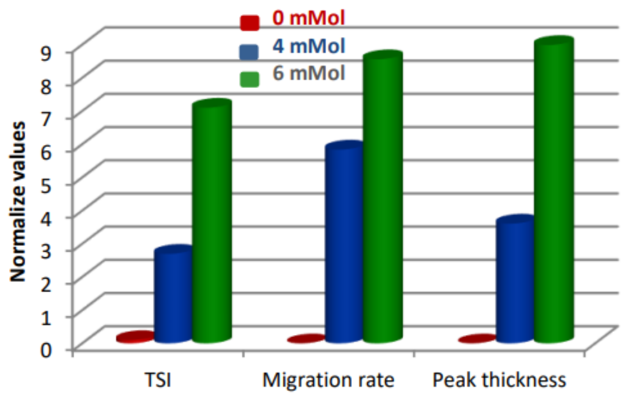
Concentration $CaCl_2$ (mMol)	Peak thickness of the oil layer (at 4 hours)	Migration rate (mm/hour)
0	0.00	0.00
4	3.61	1.46
6	8.99	2.14

Table 2. Values compute from figure 4

Using the results in Table 2, we can observe the effect of the electrolyte concentration on the migration rate of the oil droplets.

Conclusion

This application note shows a quick and simple method to characterize different electrolyte concentrations in only 1 hour. The following results are obtained.



By increasing the concentration of electrolyte, the properties of the surfactant are neutralized and so the stability of the emulsions is affected.

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