

INTRODUCTION

The Turbiscan® device is well-known for providing substantial information on the stability and dispersibility of any formulation. Such data is obtained by monitoring the evolution of the backscattered and/or transmitted light intensities over time. However, in some cases it may be difficult to objectively analyze the data without an expert eye, for example in case of simultaneous destabilization phenomena (e.g. sedimentation and aggregation). Formulation has developed a simple and robust criterium called the Turbiscan Stability Index (TSI) to rapidly compare and characterize stability of formulations. This application note describes how the TSI is calculated and provides with examples of use.

QUANTITATIVE

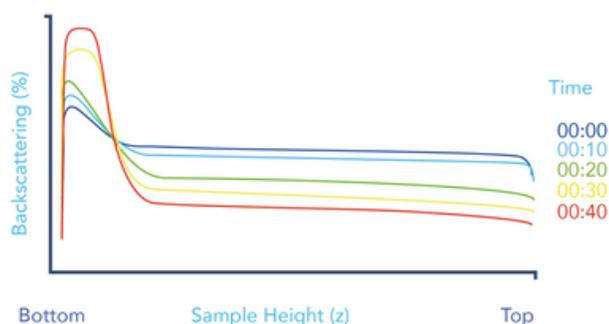
SAMPLE RANKING

FAST DECISION MAKING



Turbiscan: How It Works

Turbiscan technology is based on Static Multiple Light Scattering principle (S-MLS). An infrared light source (wavelength $\lambda=880$ nm) illuminates a sample and two sensors collect the Backscattered (BS) and Transmitted (T) signals. Both signals are directly linked to the particles' volume fraction and mean size. In addition, exploring these two signals (BS & T) allows to study a wider concentration range. The BS and T signals are acquired repeatedly over time t at the whole sample height h (scanning from $z = 0$ to $z = h$ with a step of Δh). The resulting signal is time and spatial dependent: $T(t, z)$ and $BS(t, z)$. The composition of these scans allows to detect physical instabilities in the dispersion such as aggregation, sedimentation, creaming...



TSI DEFINITION

The comparison of the stability from formulation to formulation using only the raw T or BS signals can require advanced calculation. This is why the TSI has been introduced. It is of crucial importance to classify and compare the stability of many formulations quantitatively.

Using the TSI can be done with a simple method and just one number to describe global sample stability. The TSI is a number calculated at time t by summing up all temporal and spatial variations in a considered zone :

$$TSI(t) = \frac{1}{N_h} \sum_{t_i=1}^{t_{max}} \sum_{z_i=z_{min}}^{z_{max}} |BST(t_i, z_i) - BST(t_{i-1}, z_i)|$$

with: **Tmax** the measurement point corresponding to the time t at which the **TSI** is calculated, **Zmin** and **Zmax** the lower and upper selected height limits respectively, $N_h = (Z_{min}-Z_{max}) / \Delta h$ the number of height positions in the selected zone of the scan and **BST** the considered signal (**BS** if $T < 0.2\%$, **T** otherwise).

Consequently, the sample is stable when the TSI tends toward zero and instable when the TSI is very high. Note that the TSI is equal to zero for $t=0$.

CASE STUDIES

1. Stability of nanoparticles for toxicological studies

In in vitro nanotoxicological studies, nanoparticles (NPs) must be dispersed in a cell culture medium before being administrated to cells. Classically, biocompatible proteins such as BSA are added before dispersion to coat the TiO₂ NPs and thus enhance the stability in cell culture media.

The stability of 4 TiO₂ NPs dispersions in DMEM with various BSA mass fraction has been monitored during 24h. Figure 1 shows the time dependant evolution of the transmission signal for different BSA mass fractions.

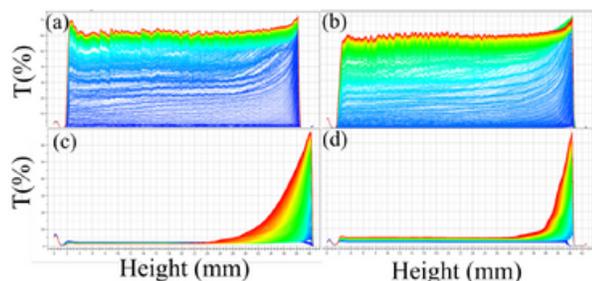


Figure 1: 24h evolution of transmitted signal for TiO₂ NPs in DMEM supplemented with (a) 0.05%, (b) 0.1%, (c) 0.2% and (d) 0.5% BSA mass fraction

Two profiles can be identified depending on the BSA mass fraction. For low BSA mass fraction [Figure 1 (a), (b)], the TiO₂ NPs dispersions are quickly destabilizing and for high BSA fraction [Figure 1 (c), (d)], the stability of TiO₂ NPs is greatly improved.

Figure 2 shows the evolution of the TSI during 24h in function of the BSA mass fraction for the four dispersions.

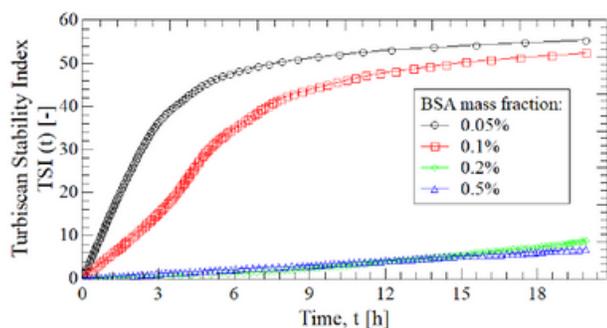


Figure 2: TSI time evolution for aTiO₂ NPs in function of the BSA mass fraction.

As observed on the raw data, two behaviours can be distinguished. For BSA mass fraction lower than 0.2%, TSI values are greater than 50 proving that dispersions are strongly unstable. For high BSA mass fraction, the TSI stays below 10 after 24h, proving that the dispersions are far more stable than for low BSA mass fraction.

2. Finding the best fragrance and concentration

Once introduced into cosmetic applications, fragrances can disrupt the cohesion and stability of end-products and lead to instabilities and customer dissatisfaction. In this study, the effect of different fragrances on a personal care product emulsion was evaluated. The objective was to identify the best dosage for each fragrance avoiding product instability. The criterium established to consider a product as stable is to reach a TSI lower than 1.5.

Following results (Figure 3) can be obtained in 2 days to rapidly distinguish and rank samples whereas usual tests are done for 45 days.

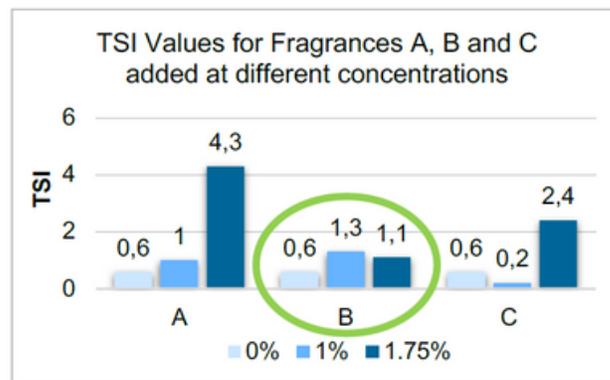


Figure 3: TSI values calculated @2days for personal care formulations containing different fragrances at various concentrations

The TSI calculation allows to display global stability in a single value allowing to simply compare the formulations. In this case it can be clearly noticed that fragrance B enables to obtain the most stable dispersion regardless the concentration used. In addition to reducing testing time the stability and thus the quality of the dispersion can be objectively determined.

CONCLUSION

The TSI is a simple and robust parameter to directly evaluate in a quantitative manner the stability of any formulation. It is a time and height independent value of the global variations of the considered signal (T or BS). It provides with a simple method to objectively compare and rank formulations based on their stability, hence providing more reliability to dispersion characterization and can be used a stability criteria