APPLICATION NOTE

Measuring Zeta Streaming Potential of Cannabis Emulsions Simultaneously with STABINO ZETA and NANOTRAC FLEX

Introduction

Microtrac's MRB Stabino Zeta (Fig. 1a) allows for the measurement of zeta streaming potential in addition to conductivity, temperature and pH. Zeta potential and streaming potential are widely used to characterize the stability of suspensions, emulsions and nanoparticles. The measurement methods for zeta potential include zeta streaming potential (Stabino zeta method, Fig. 1b) in which the liquid moves, and particles are immobilized. The zeta potential is then calculated from the relative displacement of the ion cloud, which is measured as a voltage, thus yielding the streaming potential via calibration factors (K). Conversely, the second method is via electrophoretic mobility (i.e. electrophoresis), where zeta potential is calculated from the movement of particles. However, difficulties exist from classical electrophoretic measurements such irreproducibility, bubbles, chemical environmental shifts and dilutions.

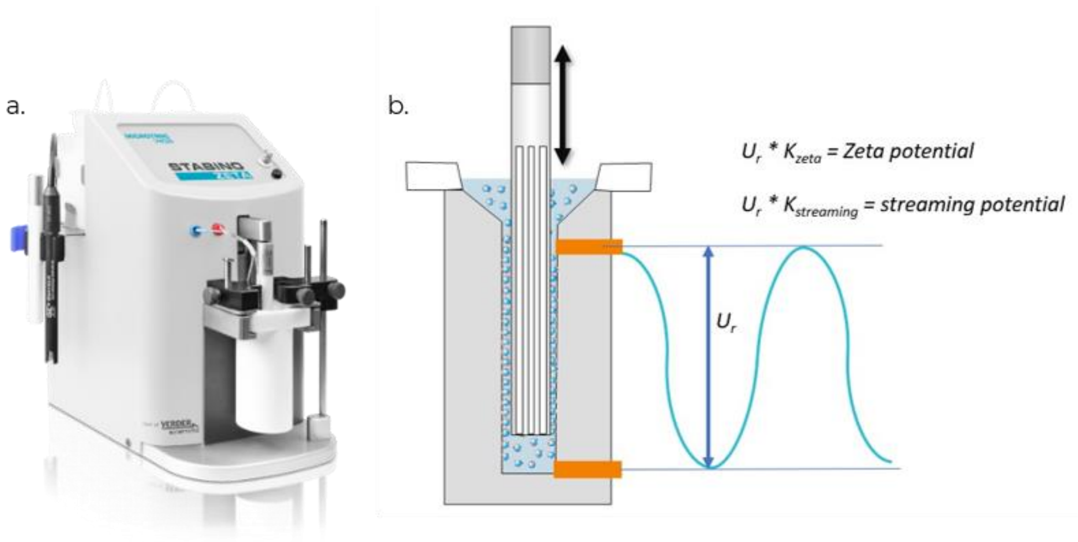


Figure 1: (a). STABINO ZETA and (b) Zeta potential calculated from relative displacement of the ion cloud measured at a voltage, U (streaming potential)

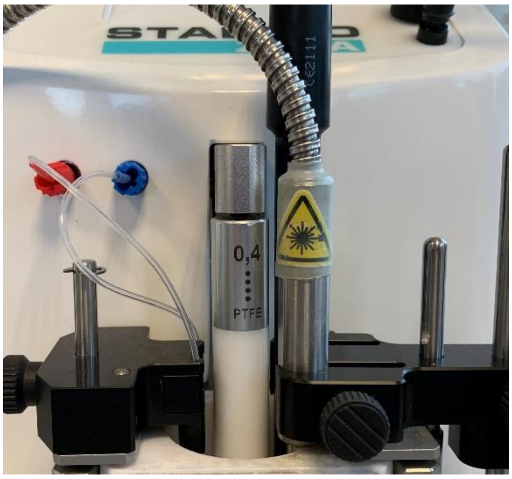
STABINO ZETA FEATURES

Titrations

The Stabino Zeta also has built-in titration functions in which all parameters are determined simultaneously at each dosing step. Titrations include pH titrations including the determination of the isoelectric point and stable pH regions, polyelectrolyte titrations to determine stability, charge density, dispersant optimization and zero point of charge and salt titrations where zeta potential is measured as a function conductivity. The entire titration or each dosing point can be followed in real time by means of the curve progression to include all five measuring parameters.

***In Situ* size Distribution**

The Stabino Zeta can also be easily combined with the Nanotrac Flex where its dip-in measuring probe can be inserted into the Teflon measuring cell of the Stabino. This feature allows the size distribution to be determined with zeta streaming potential or during a charge titration. Colloidal systems can be evaluated through the formation of agglomerations. Here we will demonstrate the combined analysis of zeta potential, particle size characterization and titration in addition to determining the isoelectric point and zero point of charge for cannabis nanoemulsions.



Experiment

Dynamic light scattering and zeta potential were used to characterize CBD nanoemulsion that were created using a microfluidizer. Five liquid solutions were involved in the creation of the final nanoemulsion with the desired particle size. The resultant cannabis nanoemulsions were analyzed using both the Nanotrac Flex and the Stabino Zeta to determine the surface charge density, stability, zero point of charge and size distribution.

Results and Discussion

The cannabis industry optimizes for quality based on the particle size of their nanoemulsions since their bioaccessability is strongly associated with particle size. Too fine or too course can severely affect the dosage, leading to variability. Here, the Nanotrac Flex DLS analyzer was used to determine the particle size distribution at each step in the emulsifying process to provide verifiable analysis. A solution of 11.0 mg/mL CBD was run through a total of five passes to achieve the final nanoemulsion. Figure 2 shows the number of passes at various homogenization pressures vs the particle size. The size of the original emulsion decreased from 330 nm to 168 nm as the number of passes increased to five. The size distribution profiles of these nanoemulsions are observed as a narrow and monodisperse and is useful in evaluating the stability in various conditions which we will be seen in the titration data.

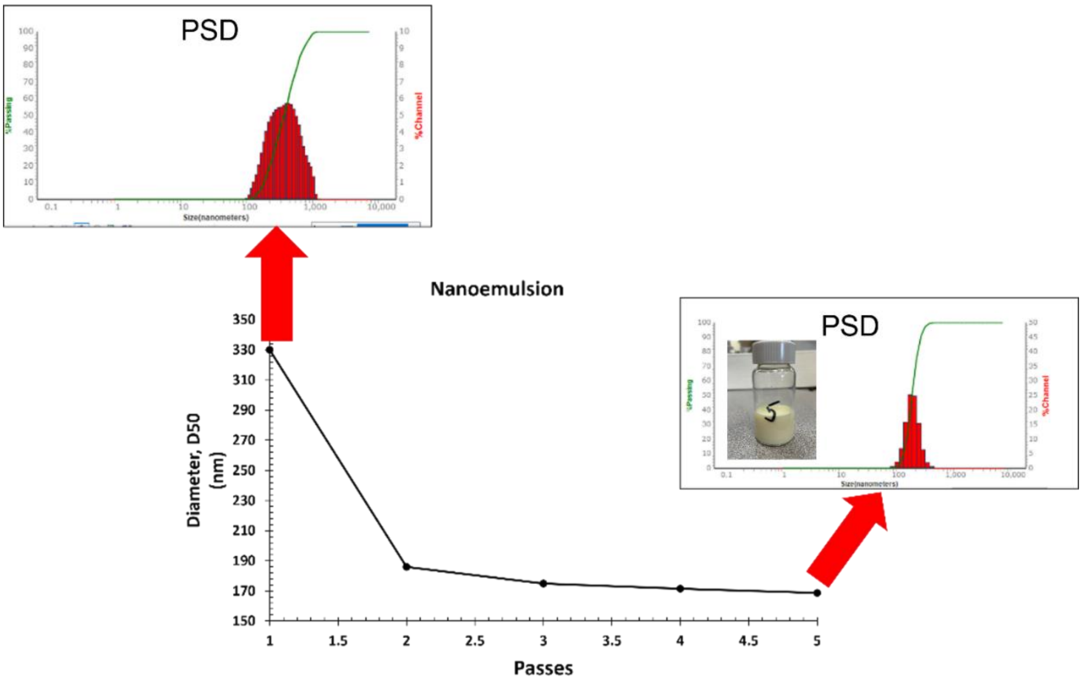


Figure 2: Particle size distribution (PSD) as a function of microfluidization passes. Pass five shows a CBD nanoemulsion of 168 nm from the original 330 nm starting solution.

Zeta potential is a method for measuring the surface charge of these oil-in-water nanoemulsions. When particles carry strongly positive or negative zeta potential, there is a strong repulsive electrostatic interaction between the particles and therefore prevents particles from forming aggregates. The prediction of the stability of these nanoemulsions were analyzed by the Stabino Zeta which provides the zeta potential via streaming potential. Figure 3 shows the mean curve of eight averaged zeta potential and pH measurements each over the course of 30 seconds. The average zeta potential and pH was -16.2 mV and 5.12 respectively.

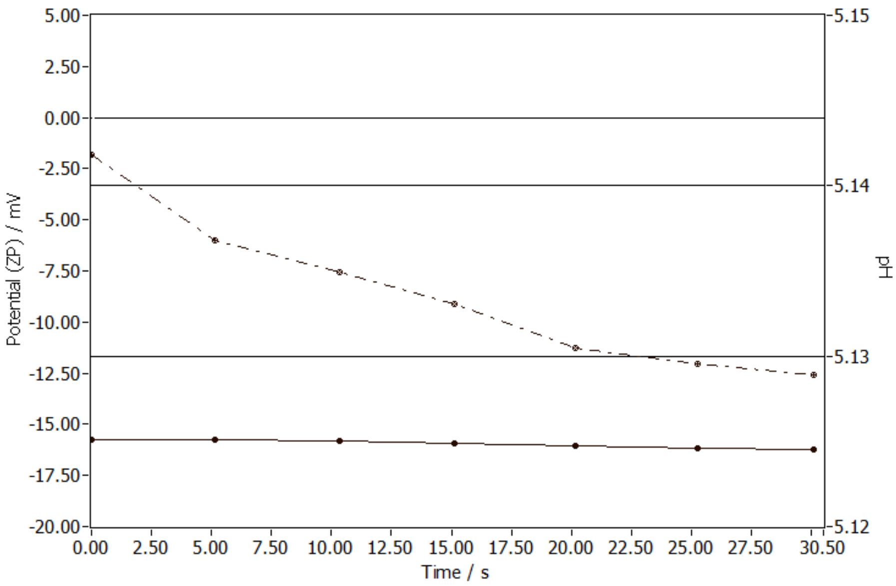


Figure 3: Average zeta potential (solid line) and pH (dashed line) over the course of 30 seconds for the resultant five-pass CBD nanoemulsion.

Zeta potential measurements are often performed in combination with titrations and at different pH values. The Stabino Zeta offers the simultaneous measurement of these parameters along with the simultaneous measurement of particle size distribution. Changing the electrolyte composition and concentration can lead to a shift in the zeta potential. Polyelectrolytes are often used to determine and directly measure the stability of the dispersions via polyelectrolyte titrations of nanoemulsions. Here, we performed polyelectrolyte titrations to influence the zeta potential and find the zero point of charge, which is where the surface of the nanoemulsion is zero. More specifically, the determination of the amount of charge necessary to overcome zeta potential repulsion which results in induced agglomeration. Since the zeta potential of the nanoemulsion was negative, a cationic polyelectrolyte, 0.001 N PolyDADMAC, a known reference standard for PE-titrations, was used.

Figure 4 illustrates the zero point of charge was achieved with only 0.62 mL positive titrant, 0.001 N P-DADMAC. The Nanotrac Flex provided size distribution data (dashed line) simultaneously as the zeta potential reached 0 mV (red line). Overall, there was an increase in size of the nanoemulsion as the surface of the nanoemulsion became zero, which is indicative of resultant agglomeration. The illustration the small amount of titrant and increase in size is clear; the solution becomes unstable as quantified by PE titration.

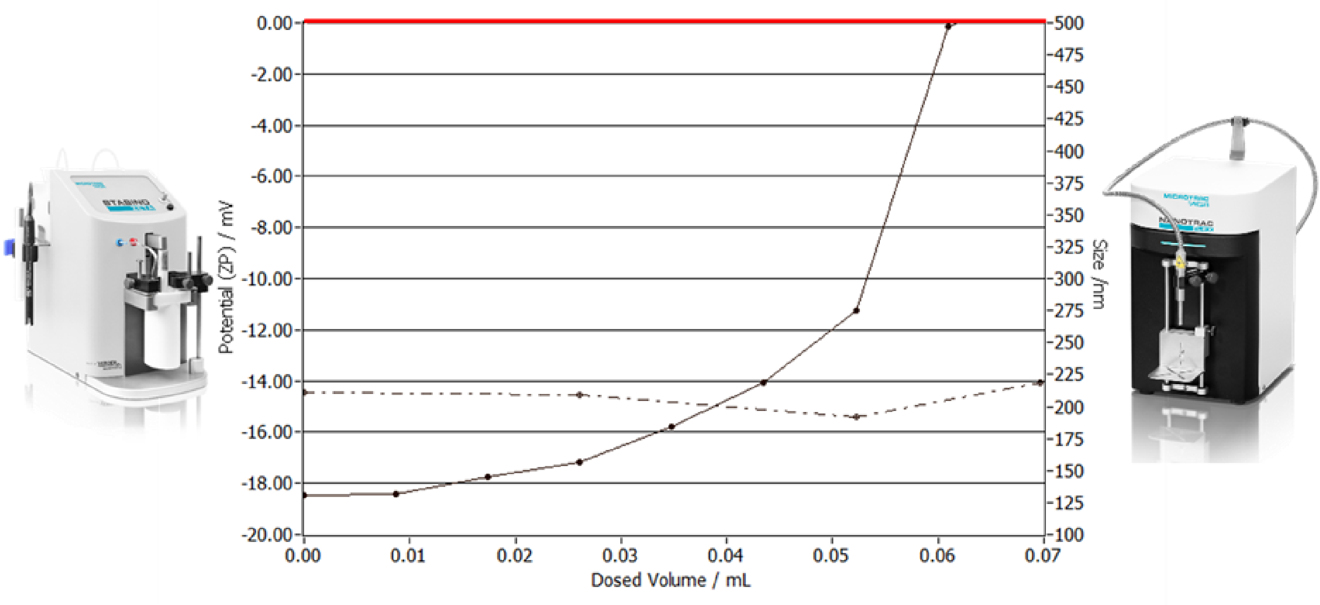


Figure 4. Polyelectrolyte titration, zeta potential (solid line) and PSD (dashed line) of five-pass CBD nanoemulsion. The zero point of charge (red line) was reached with 0.62 mL of P-DADMAC.

Summary

Using the powerful combination of the Stabino Zeta with the Nanotrac Flex we have shown the simultaneous determination of several parameters within a few seconds including zeta potential, streaming potential, pH and size range. This yields quality data about nanoemulsions' particle size distribution as a function of charge and stability, which is important in the cannabis formulation process in terms of bioavailability. Measuring the strength of repulsion and attraction was done via zeta streaming potential which rids of difficulties commonly reported from classical electrophoretic measurements.