Application Note
No. 391/2020

Spray Drying for Cannabis

Mini Spray Dryer B-290:
An approach to spray drying aqueous nano-emulsion formulations for the Cannabis market

1. Introduction

Spray-drying is a widely-accepted industrial evaporation method to produce free-flowing amorphous powders from liquid solutions. It is a well-established technology used in the commercial manufacture of products in many industries. In pharmaceutical and nutraceutical markets, spray drying is commonly used to improve the bioavailability of active ingredients within a formulation. Other benefits of encapsulation by spray drying include: enhanced product stability, taste-masking and controlled release of the drug load.

Both CBD (cannabidiol) and THC (delta-9-Tetrahydrocannabinol) derived from Cannabis or hemp plants are classified as hydrophobic compounds which display poor aqueous solubility and can taste bitter on their own. Therefore, the benefits of spray drying for the cannabis industry can be multi-fold, offering an effective means to formulate free-flowing powders from encapsulated CBD or THC oils oils, distillates or isolate which can be used for the production of edible products, dispersion into beverages, filled into capsules or compressed into tablets.

The purpose of this application note is to propose strategies and a spray drying workflow for the development of an aqueous CBD formulations (omit: "an"). An introduction to carrier oils, surfactants and encapsulant materials used for spray drying will also be presented along with nanoemulsion, nanosuspension and particle size analysis technologies which may be applied in powder formulation and testing.

2. Equipment

- Mini Spray Dryer B-290
- Standard 0.7mm two-fluid nozzle
- Outlet filter
- M-110EH Microfluidizer® Homogenizer
- Microtrac Sync – Hybrid Laser Diffraction and Imaging Particle Size Analyzer
- Microtrac NANO-flex Dynamic Light Scattering Particle Size Analyzer

3. Chemicals, Materials and Experimental

1. Full Strength CBD oil (Charlotte's Web, Boulder, CO, USA): active oil
2. Miglyol 812 (medium chain triglyceride (MCT)): carrier oil
3. Polysorbate 80: surfactant
4. Maltodextrin (DE-16.5-19.5; Sigma Aldrich): encapsulant

A series of 200 to 250-mL nanoemulsions and controls have been prepared as summarized in Table 1. Emulsions were passed through the Microfluidizer® processor equipped with a Y-type interaction chamber under desired pressure a few times to obtain a nanosized emulsion with narrow size distribution.

In formulation 1 and formulation 2, stable nanosized pre-emulsions based on water, surfactant and the oil phase were prepared with the Micorfluidizer® and stable nanosized pre-emulsions containing water, surfactant and oil phase were prepared with the Microfluidizer; multodextrin was subsequently added using a stir plate. In formulation 4, the water phase, the oil phase, surfactant and encapsulant were brought together before being processed to a nanoemulsion within the Microfluidizer®. Formulation 3 is a control consisting only of the water phase, oil phase, surfactant and encapsulant were mixed prior to processing leading to nanoemulsion formation. Resulting formulations were about 25-27 % (w/w) solids solutions at a ratio of 10:1 (encapsulant:CBD/MTC oil). Full optimization of the formulations and parameters were not done for this note.

Table 1: Experimental formulations

Sample	Hemp Oil CBD [g]	MCT Oil [g]	Polysorbate 80 [g]	Maltodextrin [g]*	Maltodextrin [g]**	H_2O [mL]
Formulation 1 MCT emulsion control	0	3.12	1.25		53	200
Formulation 2 MCT / Hemp nanoemulsion	3.12	3.12	1.25		53	200
Formulation 3 Maltodextrin control	0	0	1.25	62.5		250
Formulation 4 MCT / Hemp nanoemulsion	3.12	3.12	1.25	62.5		250

* added pre emulsion
** added post emulsion

Spray drying parameters for each formulation are provided in Table 2. Inlet air temperature (T_{in}), aspirator rate % and sample feed % were held constant, while gas atomization rate was varied. Evaporative cooling impacts the outlet temperature (T_{out}), which was observed, not controlled or set. Spray dryer process parameter settings for aspirator %, feed % and gas rates are shown in Table 2 along with their actual values which were determined using conversion charts provided in the spray dryer operation manual. Mid-range processing parameters were selected to allow room for potential optimization of spray-drying outcomes (i.e. particle size, solubility) on a per-formulation basis.

Table 2 – Mini Spray Dryer B-290 process parameters

Experiment	T_{in} [°C]	T_{out} [°C]	Aspirator [%]	Feed [%]	Gas [mm]
Formulation 1 Control MCT	170	90	90 = 35 m^3/hr	30 = 9.5 mL/min	40 = 670 L/hr
Formulation 2 MCT / Hemp	170	91-94	90	30	40 = 670 L/hr
Formulation 3 Control Malto	170	89-90	90	30	35 = 540 L/hr
Formulation 4 MCT / Hemp	170	85	90	30	45 = 830 L/hr

To determine a baseline of solubility, 250 mg samples of each spray-dried formulation were dissolved in 10 mL water at ambient temperature and observations were recorded. The particle size of the oil droplets was measured in the liquid nanoemulsion state and after dissolution of the spray dried powder in water to compare the effect of spray drying on the size distribution of the dispersed oil droplets.

4. Results and Discussion

A series of nanoemulsions were created and spray dried to identify the influence of formulation variables on finished product quality, namely particle size and ability to dissolve in water. Particle size is reported in terms of the mass median diamter (D_{50}) of the oil droplets in the nanoemulsions and of spray dried particles, respectively, as summarized in Table 3.

Table 3: Experimentally measured values of D_{50} for oil droplets in nanoemulsion, particle size of the spray dried particles as well as D50 for oil droplets after dissolution in water,

Sample ID	D_{50} of oil as nanoemulsion [nm]	D_{50} of SD powder [µm]	D_{50} of oil after dissolution of SD powder [nm]
Formulation 1 Control MCT	130-140	11.59	130-140
Formulation 2 MCT / Hemp	130-140	5.15	130-140
Formulation 3 Control Malto	N/A	7.88	N/A
Formulation 4 MCT / Hemp	90-130	5.37	90-130

Particle size of the spray dried particles was approximately 10 µm, with a range of (5-12 µm) as noted in Table 3 and displayed in Figure 1. The powder was free-flowing. The oil droplet size was unaffected during encapsulation by spray drying, as indicated by equivalent D_{50} recordings before and after the spray drying process.

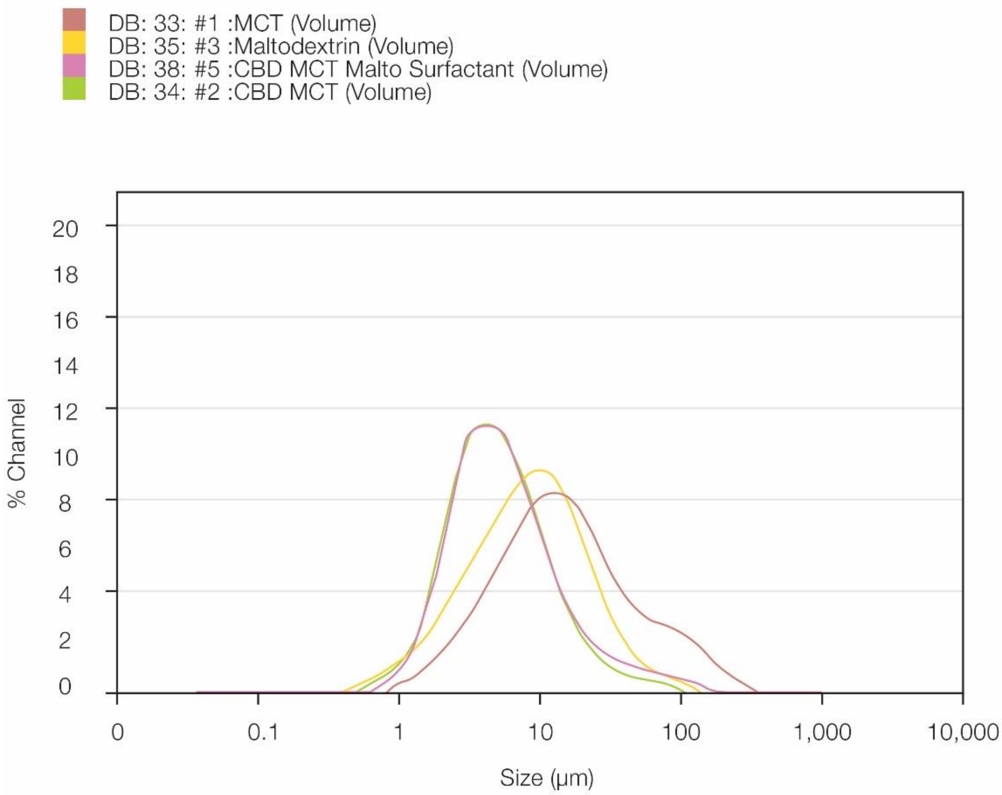

Figure 1 - Particle size analysis of spray dried powders for all formulations

5. Conclusion:

This application note provides a foundational approach to produce water soluble powders from an insoluble oil. In this example, CBD hemp oil was first made into a stable nanoemulsion in water, then encapsulate materials were added to the formulation for oil entrapment or encapsulation via spray drying to obtain free-flowing powders. Choices of carrier oils can vary, as can the surfactant and emulsifier. Selection of the encapsulate materials will be based on whether you are making edible verses medicinal products. Furthermore, encapsulation by spray drying will promote longer shelf life of cannabis oils.

Powder characteristics play a role in flowability, compressibility and dissolution performance. Changes in formulation percent solids, ratio of oil to encapsulant, as well as the process parameters used to spray dry will impact the finished particle size, bulk density and encapsulation efficiency. Please take into account the final allowable dosage of the actives for your products when formulating.

6. Acknowledgments

BUCHI would like to thank the team at Microfluidics International Corp., Dr. Yang Su, Christopher Jaquin, Kelley McCabe and Gabi Carroll and the team of RGS Scientific, Mr. Steve Rapp and Tim Jochum for their collaboration and contributing work to make the nanoemulsions and measure the particle size of the emulsions and dried powders. This application note is a success due to teamwork and everyone's insight.

7. References

1. Application Note 248/2017 Microencapsulation of Flavors and Fragrances by Spray Drying
2. Carneiro, Helena C.F., Encapsulation efficiency and oxidative stability of flaxseed oil microencapsulated by spray drying using different combinations of wall materials. Journal of Food Engineering. 115 (2013) 443-451