

<u>APPLICATION NOTE - Microfluidizer™ Technology</u> <u>compared to Ultrasonic Technology</u>

Like many other bioactive nutraceutical ingredients, cannabinoids are lipophilic, which means they are not water soluble. This caused a major challenge for the food and beverage industry when formulating cannabis oil into edible products. Direct ingestion results in very low bioavailabilities with delayed onset of the effect and prolonged period before reaching peak effect.

The low bioavailability of cannabis oil can be overcome by formulating the products into nanoemulsions. A recent study showed not only an overall bioavailability increase, but also a significant reduction in time to reach maximum plasma concentration after oral administration of CBD nanoemulsion, compared with just CBD oil as shown in Figure 1^[1].



igure 1. Plasma concentration-time curves of CBD oil and CBI nanoemulsion administered orally

Nanoemulsions are kinetically stable solutions of tiny oil droplets formed and stabilized by surfactant(s) or emulsifier(s) and dispersed in the aqueous phase. These formulations are compatible with water and can be either directly infuse into food and beverage products or dried into powders which can be reinstituted at a later time. When the droplet size drops below 100 nm, nanoemulsions become translucent or even transparent in appearance, especially with additional dilution with water which can be particularly beneficial in clear beverage applications. High-energy emulsification is usually the preferred method in industrial operations due to it's flexibility and ability to produce fine emulsions with foodgrade ingredients and at a much lower (safer) concentrations. Among various high-energy methods, ultrasonic technology, high-pressure homogenization (HPH) via Microfluidizer technology are the main methods. This application note will be focusing on providing a comprehensive comparison between the Microfluidizer technology and the ultrasonic technology.

Ultrasonication is a process that uses sound energy at high frequencies to break apart particles by cavitation — the expansion and implosion of bubbles (Figure 2). The inherent characteristics of the ultrasonic technology lead to several drawbacks:

- Contamination with metal particles (Figure 3) leads to difficult downstream processes as well as leaves a bad taste in the product
- Not suitable for continuous processing
- Not scalable to industrial scale
- Temperature control is extremely difficult
- None-uniform processing (figure 2) requires very long processing time
- The probe tip is costly and needs to be replaced often which means high cost of ownership



Figure 2. Image of ultrasonication process and schematic of intensity



Sample processed with ultrasonication method

Figure 3. Example of contaminations resulted from ultrasonication process



Microfluidizer technology ensures that fluid pressure is converted to high shear forces more efficiently and consistently (Figure 4) than is readily achievable using competing technologies. The key to the Microfluidizer technologies remarkable efficiency is the design of our exclusive fixed-geometry interaction chamber. As fluids are forced at constant pressures and controlled temperatures through the unique interaction chamber, materials experience extreme shear forces, yielding precisely controlled particle size reductions and strikingly tight particle size distribution curves (Figure 5).









	Microfluidizer Technology	Ultrasonic Technology
Technology	Constant pressure + fixed geometry chamber to achieve uniform processing.	Very high cavitational forces only near the probe tips.
Continuous	Yes!	No
Scalable	Yes - Guaranteed scalability.	No – Generally OK for very small batch size, but no real solution for industrial scale.
Optimal Temp Control	Yes – Effective and efficient cooling.	No – Very high heat/temperature generation near probe tip causes localized overheating and therefore extremely hard for temperature control.
Contamination Free	Yes!	No – Huge contamination issue with metal particles due to the erosion of the probe. Additional filtration step is required to remove contamination but impossible to remove nanosized particles that at the same scale of the actual product particles – Bad taste!
Constant Shear Rate	Yes – Results of uniform processing are efficient reduction in particle size and narrow distribution.	No – High forces near probe tips but decay quickly which results non-uniform processing. This also lead to very long processing time, e.g., hours.
Maintenance	Robust system with regular preventative maintenance - Overall low cost of ownership.	Probe has to be replaced very often due to cavitation erosion and can be costly – High cost of ownership!

Reference: 1. Y. Nakano, et al., Med Cannabis Cannabinoids, 2019 (2). © 2019 Microfluidics International Corporation

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