Solving Cannabis Consistency And Bioavailability Problems Through Nanoemulsion Technology

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ABSTRACT

The cannabis edibles and THC beverage industries struggle with consistency and bioavailability problems. This paper outlines the real and measurable benefits of using nanoemulsions in the newly growing edible marketplace. It examines the pharmacokinetic testing data, science, and research behind the latest advances in nanoemulsion technology and explores how nanoemulsions can provide greater bioavailability and improved consistency for hemp and THC products. It explains how nanoemulsion technology works with traditionally hard-to-absorb fat-soluble ingredients, like cannabinoids, to provide faster, more efficacious and consistent uptake. It also includes an analysis of how nanoemulsion technology can be used in various formats, including liquid, gummy, lozenge, beverages, and more to maximize bioavailability and dose control, decreasing the variability in effect and onset/offset times and increasing the efficacy of active ingredients.

ARTICLE

THE "SCIENCE OF SMALL" – WHAT IS A NANOEMULSION AND WHY USE ONE?

Cannabis is a highly variable, natural product that requires refining. It is a challenge compounded when manufacturers attempt to incorporate cannabis into food or beverage products, which require specific controls.

High-quality nanoemulsions can help improve consistency and bioavailability, but how can a manufacturer know if they've found a high-quality nanoemulsion?

Manufacturers typically use a liposome with water-soluble materials, which is on the left of the image below. Liposomes essentially have an oily lipid bilayer on the outside and a small core in the center where manufacturers can add in vitamin C, B vitamins, or other vitamins and minerals. However, cannabis contains fat-soluble materials, meaning that format is not helpful in cannabis products. Instead, the terpenes and cannabinoids go into the lipid phase and make up the nanoemulsion particle's core, shown on the right in the image below.

HOW TO RECOGNIZE A HIGH-QUALITY NANOEMULSION

One simple and cost-effective way to recognize a high-quality nanoemulsion is to do a visual assessment to determine if it looks milky or opaque or has gradients in color or consistency.

The nanoemulsion at the far right of the below image is clear. In the others, the lipid particles are varying sizes. With nanoemulsions, the bigger the lipid particles are, the more the visible light is scattered. That is why milk is opaque–it contains large fat droplets. As a result, when light hits it, the light scatters in all colors and in all directions and appears white.

On the other hand, if particles shrink to a very small size, as is evident in the image on the far right where the particle size is about 20 nanometers, they no longer scatter visible light; they scatter ultraviolet light. In this way, a visual inspection can offer a low-tech, easy method of identifying whether a nanoemulsion is high quality.

Figure 1.

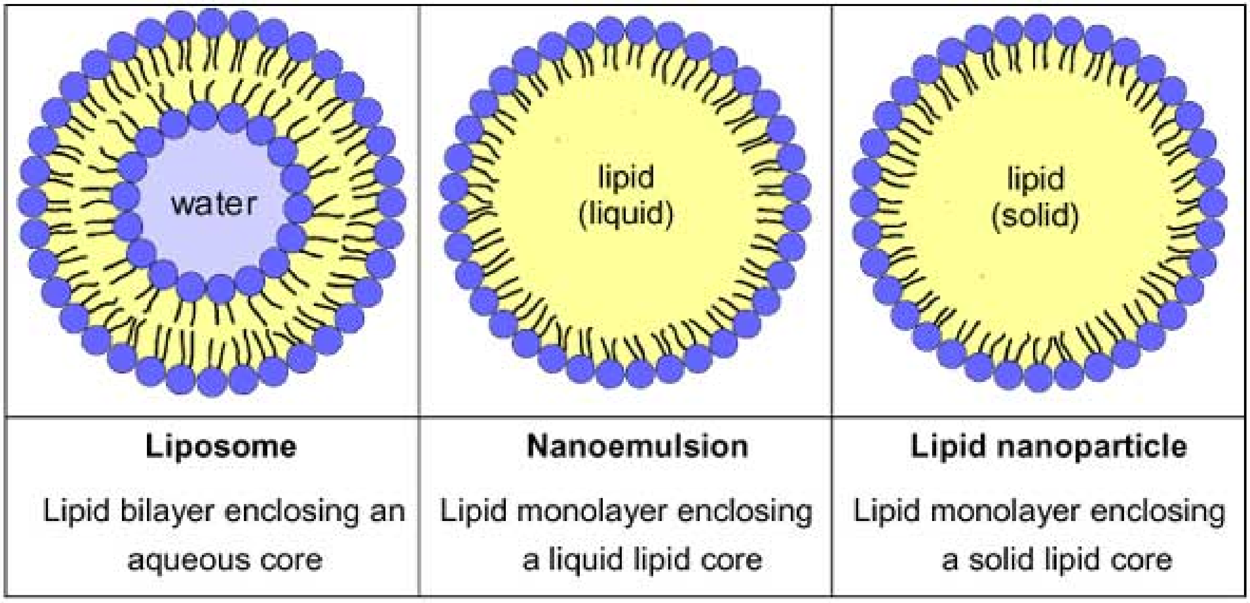


Figure 1. Phospholipid encapsulation and nanoemulsions

Figure 2.

Figure 2. A view of lipid nanoparticles of varying sizes

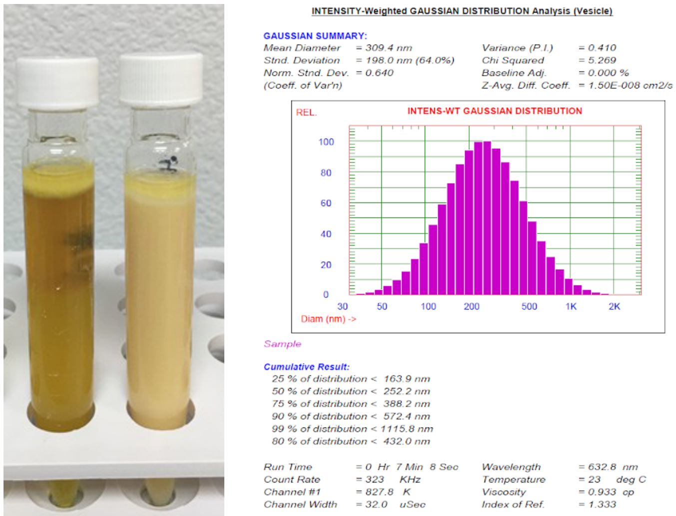
Figure 3.

Figure 3. How to recognize high-quality nanoemulsions

The second way to test the quality of a nanoemulsion is to put it in a centrifuge and spin it, subjecting the liquid to very high gravity. Large droplets have a density difference due to the liquid around them, and, as a result, they tend to separate. Correspondingly, a darker layer may appear on the top or bottom of the emulsion, depending on the density. As the pictures below demonstrate, a high-quality nanoemulsion (such as the one shown on the far right) will demonstrate no change. Well-made nanoemulsions should be clear or nearly clear, and they should also be very stable.

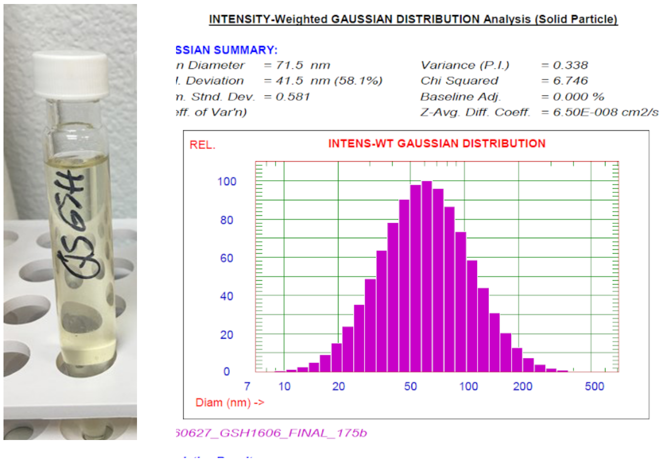
The image below shows a nanoemulsion that was milky in appearance and broke in the centrifuge. The mean diameter of the particles is about 300 nanometers, which is small but certainly not as small as one of 20 or 25 nanometers.

Figure 4



In contrast, the image below is a very clear nanoemulsion that nets out at about 71 nanometers, again demonstrating that as the size goes down, clarity and stability will go up.

Figure 5



The third method of testing the quality of a nanoemulsion is laser-scattering particle size analysis, which requires a lab. This type of scientific analysis shines light into the sample. The process essentially does the same thing as what the visible and UV light are doing—scattering in all directions at different sizes—and offers a calculation that will report the size distribution of the droplets in the sample.

A high-end analytical tool such as laser-scattering lab testing will provide much more information by probing the sample with light to determine what kind of environment the droplets are in and, more specifically, their size.

Figure 6.

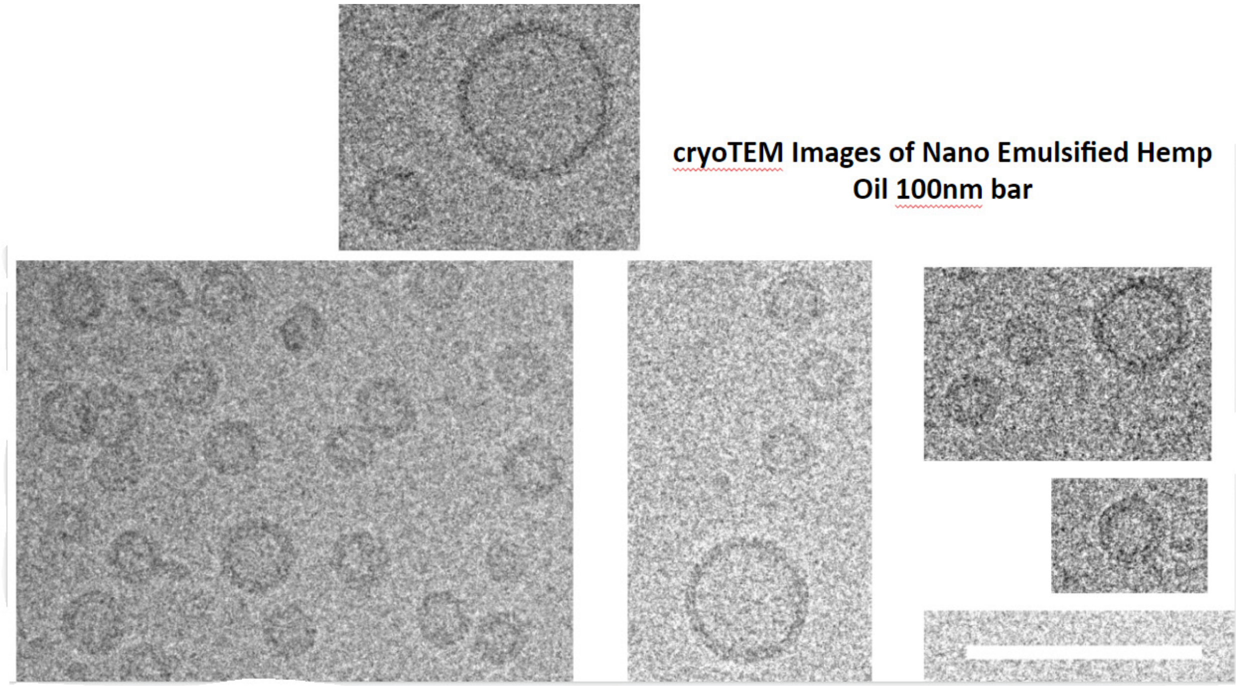


Figure 6. cryoTEM images of nano emulsified hemp oil 100nm bar

A final validation method is freezing the liquid at a very low temperature with liquid nitrogen, cutting it into slices, putting the slices into a transmission electron microscope (cryoTEM), and taking pictures. The images below are of emulsions of around 20 nanometers. The bar in the lower right-hand corner represents a hundred nanometers. In this way, the laser scattering can be confirmed with an actual visual inspection with a cryo-TEM to triple-check the quality of nanoemulsion.

At this point, evidence has established that high-quality nanoemulsions are superior and more stable. There are two types of stability in the chemical world. First is kinetic stability, meaning something is stable over time but not indefinitely. The chemicals have been pushed together into a position that over time will fall apart. The other kind of stability is thermodynamic stability wherein the chemicals are essentially stable where they are and don't want to fall apart or migrate into a different type of system. That is called a microemulsion.

An example of this is an oil droplet that is so stable that, in the right environment, it will spontaneously form a droplet and will persist to stay in that same small droplet state through all sorts of permutations, something evident in the transparent emulsions shown in the earlier images. They might look milky when the oil and water are coming together, but they snap into place and are perfectly stable and clear. That kind of ultra-stability will confer some benefits which will be outlined below.

THE BENEFITS OF NANOEMULSIONS

One of the first benefits is package stability. If the oil droplet is very stable in the environment that it's in, it's unlikely that it will find a packaging material somewhere else in the food matrix that it's happier attaching to. Although that may not be the case 100% of the time, we tend to see very robust package stability for high-quality nanoemulsions.

A second benefit is dispersibility in food matrices. Once an emulsion is very stable in its current state and has a good amount of water in it, it can be taken and dispersed into a food matrix with a very high level of consistency. So, for example, if a manufacturing facility has a beverage tank and the manufacturer

Figure 7.

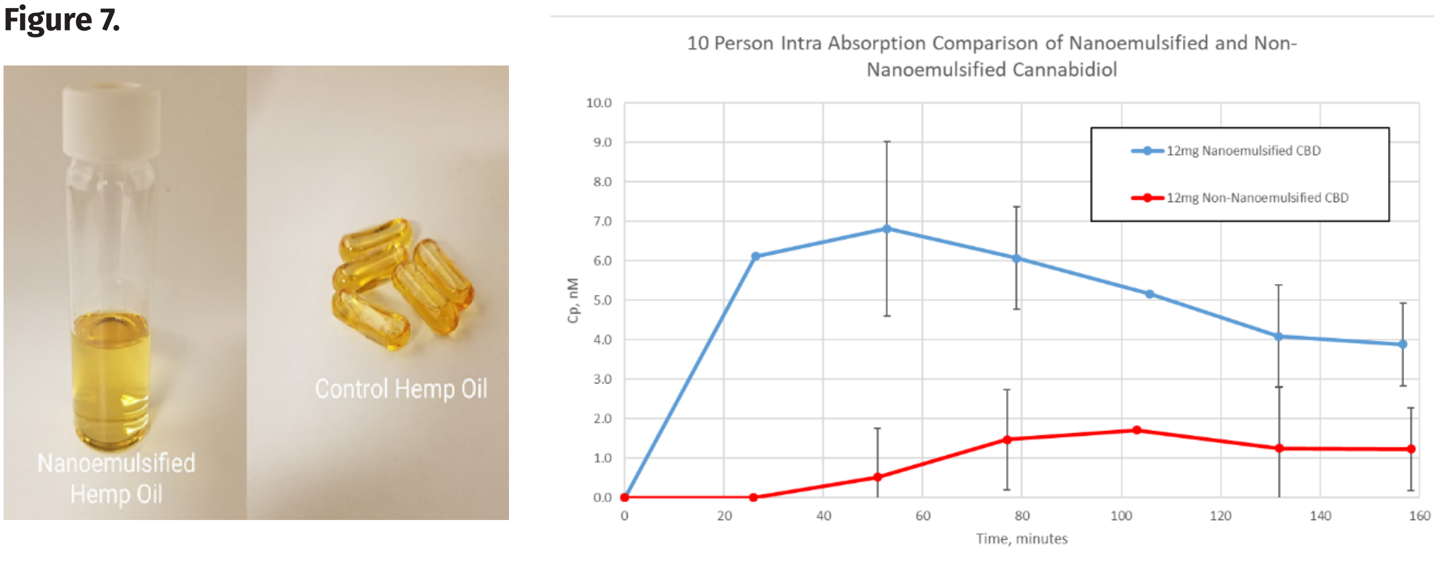


Figure 7. Intra-absorption comparison of nanoemulsified and non-nanoemulsified cannabidiol

needs to ensure that the active ingredients get completely dispersed throughout the tank, this type of nanoemulsion will be able to be very uniformly and readily dispersed from top to bottom and side to side.

Finally, high-quality nanoemulsions offer excellent physical stability. As long as the manufacturer does a great job of making a robust system that will survive the processing, the droplets will be so stable in their macro-environment *and* their micro-environment that when they're dispersed into a food matrix they will stay in that conformation.

For example, once the emulsions pictured earlier dissolve into a food matrix (be it a gummy, lozenge, or confection), it's possible to use light-scattering particle analysis to confirm that the nanoemulsions were 20 nanometers when they went into the hot sugar, and they remained 20 nanometers when they came out in the finished product. So that can be an excellent test of product formulation.

Nanoemulsions can make very stable, consistent products, but what about their performance? Putting cannabinoids and terpenes into edibles is a tricky business. It is difficult to differentiate one brand from another and stand out—the marketplace can be reasonably flat. However, the superior performance and uptake offered by a high-quality nanoemulsion allow the opportunity to do just that.

MEASURING NANOEMULSION PERFORMANCE

The best way to measure performance is through human uptake studies, in which people consume the product and then have their blood drawn over time. That is a very objective way to determine whether a product is doing what it claims to do.

Another option is Caco-2 GI permeability assays, where a layer of cells separates two liquids, and the test measures how fast the materials migrate from one liquid to the other. Those are great, but they're relative because they can only indicate that product X is better than product Y, and can't specifically show how long the update takes and what happens after. So the preferred testing method is to use a blood draw.

The images below chart people who have come to the Quicksilver Scientific clinic, consumed the materials being tested, and had their blood drawn over time. Then their blood is put into a quadrupole mass spec to measure the nanograms or nanomolar concentration of cannabinoids in their blood.

The nanoemulsion seen above is clear. Next to it is an unemulsified hemp oil which was used as a control. It is pictured as a capsule but was administered as a liquid. In this test, a few drops of very precisely weighed liquid of each type of hemp oil were administered to the test subjects.

The graph demonstrates a tremendous difference

Figure 8.

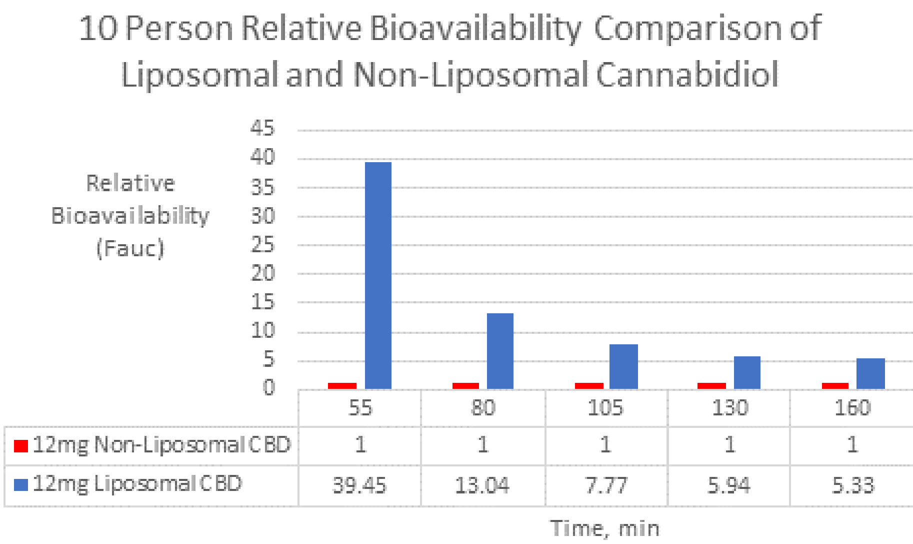


Figure 8. A comparison of the relative bioavailability of liposomal and non-liposomal cannabidiol

Figure 9.

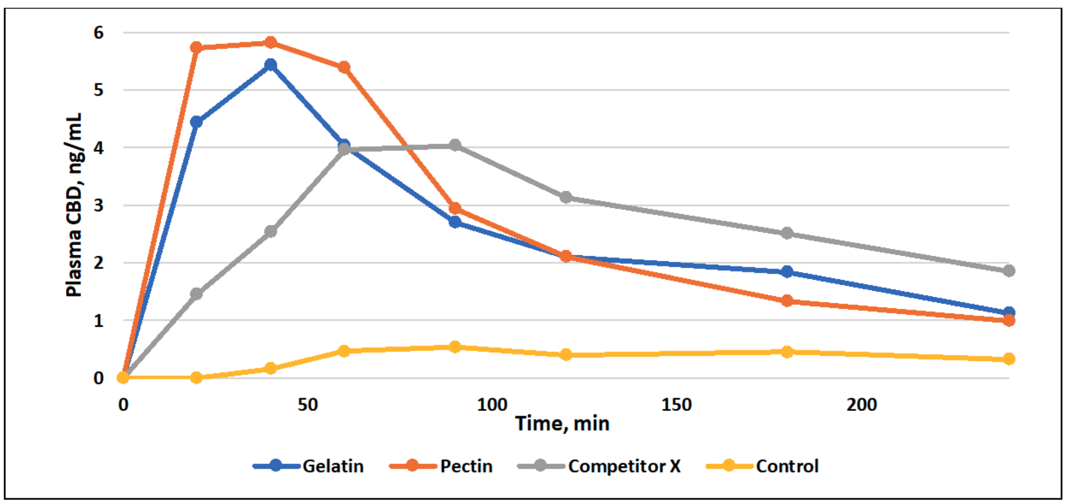


Figure 9. Pharmacokinetic data: CBD gummies

between the 20-nanometer droplets and the control hemp oil. In the blue line, it is evident that the concentration of CBD goes up quite quickly with the nanoemulsified option and peaks around the 45-minute mark; however, the hemp oil never really offers much in the way of performance.

It's evident then that the bioavailability and onset of the nanoemulsion are much better, partly because, as stated earlier, it simply takes longer for the body to break down and absorb bigger fat droplets. Only when the droplets are sufficiently tiny can they be metabolized and absorbed properly.

Using a 20-nanometer droplet means skipping right to the end of the more time-intensive absorption process by presenting the body with something that, although not instantly digestible, is infinitely more digestible than something bigger. When properly made, the same results can be replicated in confections or different gummy formulations.

The study shown above evaluates the effectiveness of nanoemulsion technology in delivering a 12 mg dose of CBD in two different gummy bases: gelatin (blue line), and pectin (orange line). The absorption of both gummy formats with the nanoemulsion is then compared to the uptake of a well-known CBD gummy (grey line). Again, it's evident in both the pectin-based gummy and the gelatin-based gummy that when using the nanoemulsion the bioavailability increases and the performance is better. In addition, they offer speedy onset and not just better performance relative to oil, but better performance relative to other gummies on the market using this kind of technology.

CONCLUSION

Smaller nanoemulsions lead to excellent uptake and bioavailability. As the pharmaceutical industry knows quite well, it's a wasted effort if the body can't absorb whatever it's ingesting. As a manufacturer, why take the time, effort, and money to make a great edible or drinkable product when the key ingredient is delivered in a format that cannot be readily absorbed?

Nanoemulsions offer faster effects and more efficient bioavailability and can offer manufacturers a real advantage in a competitive marketplace. They also ensure that the products will deliver a more rewarding and consistent consumer experience, which in turn encourages repeat purchases. Manufacturers should not underestimate the value of providing consumers with a consistent product experience where the consumer trusts and understands the outcome they can expect from a given product.

Using high-quality nanoemulsions also means that manufacturers will spend less money on pricey key ingredients due to improved bioavailability and potency. Overall, high-quality nanoemulsions offer manufacturers a strong point of differentiation and a more potent, bioavailable, and consistent experience for consumers.