



## Particle Characterization of Nutraceutical Products

**Nutraceuticals are food extracts that have been demonstrated to produce a physiological benefit or provide some protection against chronic disease. As the name implies, nutraceuticals are the intersection of nutrition and pharmaceutical and is an umbrella term that can also include functional foods and dietary supplements. In the same way that the particle size and shape distributions of active pharmaceutical ingredients and drug delivery systems effect their solubility and bioavailability, so is particle characterization critical to nutraceuticals. Laser diffraction particle size analyzers offer the same benefits in speed, precision, and reliability to nutraceutical materials that have made the technique popular in the pharmaceutical industry.**

### Introduction

Nutraceuticals are the children of nutrition and pharmacy, born of the 21st century's growing emphasis on healthier living through science. The natural progression of food science has taken nutrition out of the kitchen and into the laboratory where it can use the knowledge base already developed by a successful, mature pharmaceutical industry.



Nutraceuticals possess certain qualities that promise consumer popularity as well. Culturally, there is an ongoing shift towards purchasing naturally derived goods and drugs and this shift lends a "cure preference" to nutraceuticals as opposed to pharmaceuticals. Additionally, the typically high cost of drug discovery (which in turn leads to high cost prescription drugs) is mitigated given the narrowed scope of active nutraceutical ingredients. Many foods already provide empirical evidence of imparting disease resistance to the consumer. The challenge is to identify which components of healthy foods

make them so, but with the advantage that the active ingredient location is confined to the food. To this end nutraceutical, pharmaceutical, and biotechnology companies have committed billions of dollars towards the research and development of commercially available foodstuffs that are both biocompatible and bioavailable.

### Particle Size Analysis

Nutraceutical compounds don't yet fall under the same regulatory guidelines and control known to the pharmaceutical industry, but many of the same analytical studies are conducted regardless. Quantitative particle size analysis provides information that has either a direct effect or correlation to issues such as bioavailability, solubility, and quality control. Of the sizing techniques currently available, laser diffraction is the most popular and ubiquitous for the size range commonly applicable to nutraceuticals. The case studies that follow all feature particle size distributions generated by the HORIBA LA-950 - a laser diffraction instrument (Figure 1).



Figure 1: LA-950 Particle Size Analyzer



### Application: Bioavailability of CoQ10

Coenzyme Q<sub>10</sub> (known by many other names and abbreviated as CoQ10 herein) is an oil-soluble compound and a participant in the electron transport chain and aerobic cellular respiration. Critically, CoQ10 acts as an antioxidant that the human body synthesizes in decreasing amount over time. Typically, the elderly and/or diseased body struggles to manufacture sufficient CoQ10 which has created a market for the compound as a vitamin supplement.

Befitting the important role it plays in the body's natural energy production cycle, CoQ10 is one of the more heavily researched nutraceuticals and promising results have been observed on a number of fronts such as improved heart muscle performance, improved pulmonary capacity, and lowered hypertension.

A challenge in formulating CoQ10 supplements is the intrinsically low bioavailability of the hydrophobic, high molecular weight compound. Lipid solubility is also limited which rules out the gastrointestinal tract as a location of efficient absorption. Typical absorption of CoQ10 requires emulsification and micelle formation, but this process may be altered through the reduction of particle size.

Using nano-scale particles as a drug delivery system has long been researched for drugs with poor absorption characteristics. Changing the drug's size profile also changes the absorption pathway and may lead to higher efficiency. Another approach to improving bioavailability is to use the typical gastrointestinal pathway and increase efficiency simply through careful oil emulsification before ingestion. These two particular methods are compared via particle size distribution in Figure 2. The LA-950 particle size analyzer was used to characterize both the approximately 100nm nanoparticle formulation and the macro-emulsion with median diameter greater than 100 $\mu$ m.

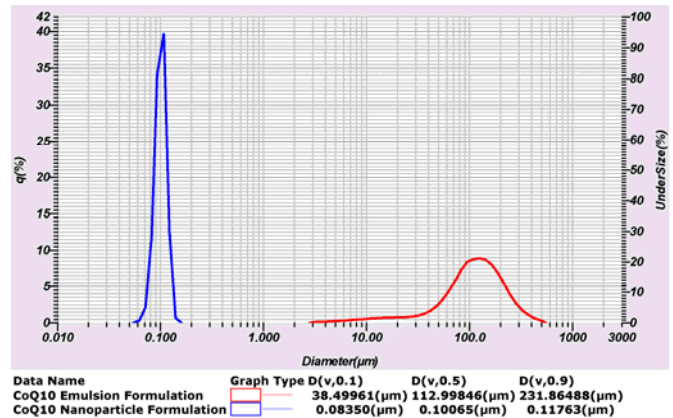


Figure 2: Particle size comparison of two CoQ10 formulations

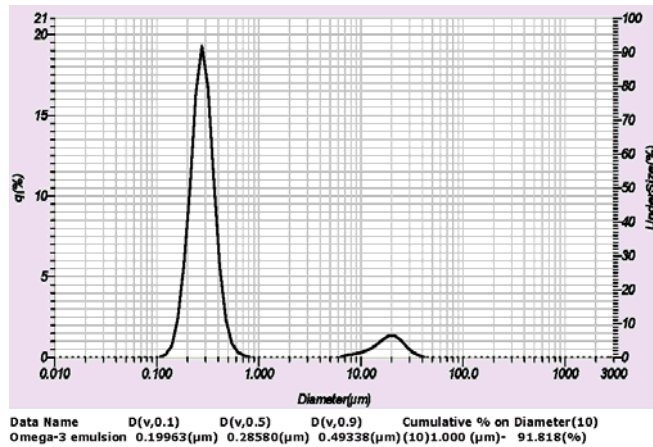
### Application: Quality Control of Omega-3

Omega-3 fatty acids are a group of nutraceuticals which enjoy both a high degree of public exposure and promising clinical trial data. These compounds are a family of unsaturated fatty acids that possess a common carbon-carbon double bond in the n-3 (i.e. omega-3) position. Nutritionally essential omega-3 fatty acids include alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). The body can synthesize long-chain omega-3 compounds from an ALA precursor, but this process is inefficient compared to food ingestion. Prevalent sources of omega-3 compounds include cold water fish such as tuna and salmon and a newer discovery, microalgae.

Supplementing a traditional diet with omega-3 fatty acids has shown promising evidence of reducing coronary heart disease risk. Given that hundreds of thousands of Americans die every year of heart disease the surge in consumer popularity and research into the effects of omega-3 are directly explained. Potential additional benefits in such diverse areas as arthritis, depression, attention deficit disorder, and cancer prevention are the objects of intense evaluation as well.

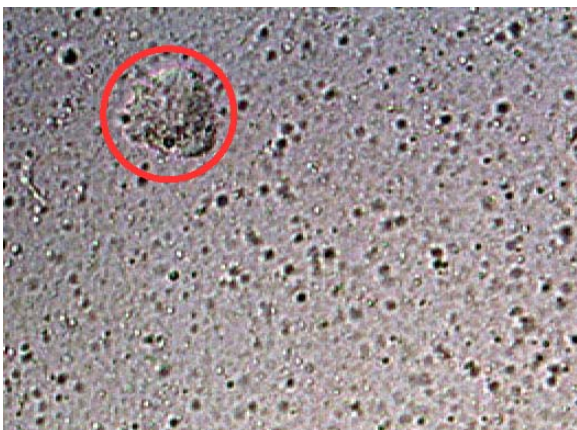


Figure 3 shows the particle size distribution of an Omega-3 fatty acid (specifically DHA) emulsion formulated for off the shelf consumption. This particular sample features a small, but significant population of large particle contaminants.



**Figure 3: Omega-3 emulsion contaminants**

The manufacturing process was designed to eliminate large solids greater than 1µm, and as such this result qualifies the batch of material as failing. The analysis tells us that 8.2% of the particle size volume is larger than the critical size. The accuracy and resolution of the LA-950 particle size analyzer used were verified with optical microscopy and a representative image is shown below in Figure 4. Most laser diffraction based analyzers are capable of detecting even smaller quantities of contaminants with the best instruments resolving volumes less than 1%.



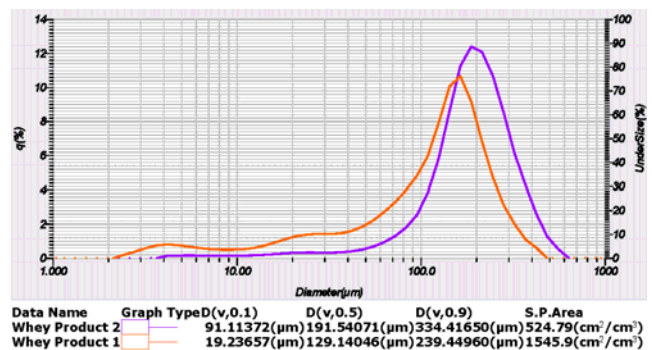
**Figure 4: Verification of large particles using optical microscopy**

### Application: Solubility of Whey Protein Isolate

Whey protein is commonly used as a dietary supplement either to counteract protein deficiency or to accelerate muscle development and recovery. Popular among fitness enthusiasts, whey is an excellent source of protein with high *biological value*. This refers to the proportion of absorbed protein which is incorporated into the body's protein supply.

Whey powder has little to no flavor and thus is mixed into solid and liquid foodstuffs. Typically the whey powder is dissolved into a liquid such as milk which raises the question of solubility from two fronts: ease of use and absorption profile. The first is a measure of the consumer's willingness to expend effort dissolving the protein over time. The latter is a measure of how much of the ingested protein is absorbed by the body at which point the biological value of the protein determines incorporation.

Generally, increasing surface area improves solubility characteristics, and this may be accomplished through the reduction of particle volume and thus particle diameter. The particle size distributions of two different whey protein products were analyzed on the LA-950 PowderJet dry powder accessory to determine the correlation between particle size and solubility concerns (Figure 5). The PowderJet allows the powder to be analyzed in a dry state, removing solubility as a variable in particle size determination.



**Figure 5: Particle size of two whey products and the effect on specific surface area**

**Conclusions**

Time, money, and effort are being devoted to “natural” remedies for their minimal side effects and low cost in comparison to pharmaceutical drugs. These nutraceuticals enjoy the benefits of positive public perception, increasing exposure, and empirical evidence from so-called “super foods”. We can readily observe the importance of particle characterization to the nutraceutical industry as this information impacts research and development concerns as well as quality control in the previous examples. Laser diffraction based particle size analyzers bring the same benefits to nutraceutical measurement that make the technique popular among the pharmaceutical industry:

- Fast analysis time
- Excellent precision
- Wide measurement size range from nanometers to millimeters
- Sample handling systems for every application
  - Suspensions
  - Emulsions
  - Dry powders
  - Limited or precious sample quantities
  - Viscous samples
  - High-throughput automation

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For further information on this document or our products, please contact:

HORIBA Instruments, Inc.

17671 Armstrong Avenue

Irvine, CA 92614 USA

1-800-446-7422

[labinfo@horiba.com](mailto:labinfo@horiba.com)

[www.horibalab.com](http://www.horibalab.com)