



# INSIDER™

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## Athletes Seek a Nutritional Edge

Forever at the forefront of the nutrition industry are sports-minded consumers, especially athletes. Even in area where research is slow to validate benefits, sports nutrition fans will try almost anything with potential to improve their bodies and performance abilities at a safe but swifter pace than plain ol' eating and working out. Well-researched sports staple ingredients such as creatine, protein, glucosamine and antioxidant vitamins and minerals are still doing well, alongside up-and-comers like tribulus, Tongkat ali, *Citrus aurantium* and 7-keto-DHEA.

*Story begins on page 22*



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## It's a Bird, it's a Plane, it's SuperFruit!

Fruit has always been a health savior, and the benefits of standbys like cranberries and blueberries can't be denied. However, standard ingredient offerings are gaining company from a group of nutrient-dense fruits from exotic locales. These increasingly popular superfruits are richly colored and chock-full of healthy phytonutrients, including potentially powerful antioxidants. Noni, mangosteen, goji, açai, camu camu and pomegranate have stormed the market, showing up in a bevy of pills, foods and drinks. The story behind these superfruits is indigenous, the research slow. But consumers are clamoring for the new hot ingredients, leading suppliers to get innovative. Some are using processing methods such as freeze drying to deliver the whole fruit in an ingredient form; others are isolating bioactives to ensure efficacious levels of compounds used in research trials. And both paths are facing bumps in the road in delivering quality through the finished product form, whether food, beverage or supplement.

*Story begins on page 44*

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# Capitalizing on Encapsulation Technologies

From hard-shell and soft gel to microencapsulation, options abound to help find the best delivery form for any given supplement formula. The technologies and innovation in encapsulation are being driven by new, challenging demands from formulators and consumers. The expanding popularity of functional foods and beverages has presented many challenges to incorporate ingredients that have little history in most foods or drinks. Among these issues are taste, color, stability and bioavailability. Another area of piqued interest is certification, as people begin to tune into kosher, organic and vegan/vegetarian designations as not only symbolic of better health but also indicative of higher quality standards.

*INSIDER* discusses the topic of encapsulation innovation with four of the leading companies in this field—Capsugel, Soft Gel Technologies, Qualicaps and **Robinson Pharma**. Also check out the article on page 56 for a detailed tour of the finer points of the encapsulation process.

**INSIDER:** *What are the significant recent innovations in encapsulation, including technologies and equipment?*

**Robert Whitelaw, director of sales, marketing and business development for the Americas Region, Capsugel:** Liquid filling of hard capsules is probably the technology that has really taken off recently with notable presence now in the dietary supplement and nutraceutical markets. Weight loss, sports nutrition and women's health are all markets that have seen notable additions in this dosage form. While the technology has existed for some time, recent innovations to equipment, like the Bosch 1400 L, have allowed for more viable commercial speeds. Liquid encapsulation microspray sealing technology—or the high speed sealing of liquid-filled capsules without banding—is part of the reason for growth of this dosage form.

Nanotechnology and micro-emulsions are now being used to reduce particle size of active ingredients and deliver them in a form more readily absorbed by the body. We are also starting to see work on the delivery of multiple dose formats including both liquids and solids in a single fused capsule.

For powder-filled capsules, new higher speed capsule filling machines are allowing manufacturers to produce quality capsule products at a higher speed, lowering the cost of encapsulating. Custom "trade dress" such as natural colorants and printing are showing up more in the "natural" supplement category. Marketers are looking for ways to set their products apart from others. Custom colors and printing allow customers an option to provide a beautiful, elegant dosage form.

**Ron Udell, president, Soft Gel Technologies Inc.:** There are extrusion methods allowing for more powders and a more solid fill to be put into softgels. Also, chewable gelatin capsules have been developed. Offering this type of softgel provides branders with the opportunity to market a product to those target populations who have difficulty swallowing—particularly the elderly and children. The fill material can be flavored to mask any undesirable tastes.

Enteric coating is a technology available for soft gel capsules, which is beneficial for certain applications where delivery of the active substance bypasses gastric juices in the stomach and is absorbed in the intestinal tract. Fish oil, garlic, peppermint oil and oregano oil are prime examples of enteric coated nutritional products available on the market, as they help mask unpleasant odors and tastes, and prevent irritation of the stomach lining.

**Brian Jones, scientific advisor, and Tamara Smith, head of marketing, Qualicaps:** The key word here is "recent". If taken literally, the only innovations that meet the criteria are liquid fill and seal machines for low viscosity formulations. There have been several machine innovations that enable liquids to be filled into two-piece capsules. Liquid filling equipment can fill materials at viscosities between 100 to 1000 centipoise.

## The 411 on Enzymes and Microencapsulation

by Lisa Clark

With the convergence of the dietary supplement and food industries, the term encapsulation has created a bit of confusion. The manufacturing of vitamins, herbs, enzymes and other raw materials placed within a two-piece hard-shell (gelatin or vegetable) capsule is referred to as encapsulation. However, in food manufacturing, encapsulation relates to particulate manipulation, as in an outer coating (usually a lipid) normally applied to improve stability, delay release of a nutrient, or to taste mask a material within a food. This is known as microencapsulation.

Enzymes are not living organisms, are very stable under ambient conditions, and are fairly tasteless and odorless. While we don't want to completely rule out the development of microencapsulation technologies for digestive enzymes, we must analyze the benefits of the application carefully. Enzymes are catalysts to reactions and must be available when they meet their substrate (the compound to be catalyzed). If enzymes are bound within a lipid or other coating, as in microencapsulation, a few questions must first be answered. How does the body (digestive system) "peel off" the coating to expose the enzyme? Under what conditions? In what timeframe?

Despite these issues, the greater question might be: *Would there be an advantage to adding a microencapsulated enzyme to a powdered protein drink mix, if we want the enzymes to activate immediately upon ingestion (in the stomach) to free the amino acids of the protein before absorption in the small intestine?*

Supplemental enzymes are still used primarily for digestion among mainstream consumers and the stomach is still the best place for digestion to occur. Our best delivery systems currently are capsules and tablets.

*Lisa Clark is the director of marketing and business development for the West coast division of Deerland Enzymes.*



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**INSIDER: How is your company contributing to encapsulation innovation?**

**Whitelaw:** Liquid encapsulation microspray sealing technology—the high speed sealing of liquid-filled capsules without banding—is part of the reason for growth of this dosage form. It is a patented process, LEMS™ technology, and was developed to securely fuse two-piece liquid filled Licaps® capsules using the LEMS™ 60 machine. This high-speed production-scale sealing machine eliminates the need for banding, sealing up to 50,000 capsules per hour with a precise microspray of hydroalcoholic solution that fuses the body and cap of the capsule into one unit.

**Udell:** Soft gel capsules can be used to improve bioavailability by delivering the nutrient in solution or other absorption-enhancing media. The advantage to small particle or crystal size is that the smaller the particle, the better and quicker it is absorbed in the digestive tract. By providing enhanced absorption and bioavailability, consumers can expect fast disintegration and immediate nutrient delivery to produce a quicker onset of action. Better bioavailability also translates to a possible reduction in the required dose of the active compound. CoQsol-CF™ is a crystal-free, solubilized softgel coenzyme Q10 (CoQ10) formulation offered exclusively by Soft Gel Technologies, clinically studied to show a higher rate of absorption over CoQ10 powder.

Also, soft gel capsules can accommodate a wide variety of compounds filled as a semi-solid, liquid, gel or paste. Also, more emulsion and micro-encapsulated materials are being put into soft gel capsules, making them more functional and giving a greater variety of choices as to availability and dosing. Micronized materials can be used in inner fills of soft gel capsules, whereas tablets and hard-shell capsules require larger particle sizes, so that the powder will flow in the tableting or encapsulating machines.

**Kenn Israel, vice president of marketing, Robinson Pharma:** Robinson Pharma is proud to be the first softgel manufacturer to convert its facility to 100-percent continuous drying capacity. Rather than use the standard tray drying technology that has dominated the industry for the last three decades, we've implemented an innovative system that reduces the average drying time of a softgel to 20 hours from the traditional three days. This dramatic improvement in throughput saves energy and time and allows for a more consistent and reliable product.

**Bob Brosnan, director of nutritional business development, Qualicaps:** The two capsule technologies that Qualicaps is most excited about are liquid filled capsules and Quali-V® HPMC (hypromellose) non-gelatin capsules. Qualicaps feels demand for both of these categories will continue to trend upward in the dietary supplement industry.

**INSIDER: How has the growth and boom of functional foods and beverages challenged encapsulation operations (taste/ flavor, dispersion, interaction between ingredients, etc.)? And, how has the encapsulation industry responded to or addressed these challenges?**

**Israel:** Functional foods are proving one can have a pleasant experience while consuming an active ingredient. It is clear the customer demands a product experience that goes beyond taking a pill. Interest has increased in innovative delivery systems such as effervescent tablets, rapid melt tablets, and fragrances and flavors for encapsulated products. Robinson Pharma has been active in creating delivery technologies that go beyond the traditional and basic to include pleasant flavor, visual, fragrance and texture experiences.

**Whitelaw:** Supplements are viewed more and more as a natural extension of functional foods. They represent the opportunity for the benefits of functional foods in more convenient, portable and focused forms. For example, if you want the benefits of omega-3s but don't like the taste of tuna fish, supplements provide the solution. In the past, people may have consumed a product deemed healthy even if it tasted bad. Today's consumers expect products to have an acceptable taste. The challenge for functional foods/beverages is in developing efficacious products that taste good, are stable over time and deliver enough of the active to support the marketing claim. That's where supplements work.

**Udell:** Customers are increasingly asking for flavored fill materials and/or gelatin shells as a way to differentiate their products and promote consumer satisfaction. Soft Gel Technologies currently adds flavors to the gelatin and/or fill, and has experience in doing both. Products today have increased functionality—they use a greater combination of ingredients to reach the various targets that the products are aiming to address. There is also a greater demand for manufacturing products with new combinations of materials. Many of these ingredients can interact with one another, causing a possible decrease in activity of one or more of them. Combining multiple ingredients can also create reactions that cause the fill to become difficult to work with during the production stage of encapsulation.

**INSIDER: How, then, is the issue of interactions within functional products best addressed?**

**Udell:** We investigate any possible interactions in our formulations prior to finalizing them. This allows us to address ingredient compatibility issues—such as function, stability and/or processing problems—and make any necessary formula changes to correct or avoid any of these potential problems. There are various ways to deal with these issues. By using a different form (physical or chemical) of the ingredient(s), which will not be as susceptible to these interactions, we avoid these problems. Some materials may be chelated rather than in free form, or may be microencapsulated to protect them. Sometimes, adding a small amount of an otherwise inert ingredient can protect one or more of the ingredients from interacting with the others. Our technical staff stays current by reading literature that provides new information regarding these possible interactions and how to prevent them from occurring. If no published research is available on a certain material, our scientists perform trials in the R&D lab to discover ways to minimize or correct these undesirable properties.





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**INSIDER: Which ingredients, especially the more recently popular, are the most challenging to encapsulate?**

**Brosnan:** Any hygroscopic (water-seeking) fill material can cause challenges. In addition, many mineral products, which tend to be coarse and “gritty” also pose challenges. Both of these can degrade the capsule shell.

**Whitelaw:** Any liquid or hygroscopic material presents issues regarding both seal integrity as well as the potential for oxidation and brittleness. In our LEMS process, we fill in an oxygen-free environment using a nitrogen blanket and nitrogen flush before the capsules are microsealed. Capsules have low oxygen permeability because they do not contain plasticizers—especially when compared to softgels with plasticizer channels that result in very porous products. Liquids sealed in the capsule are better protected against oxidation and less likely to transmit odors than those in softgels. This is especially important when the purpose of the encapsulation is to mask offensive tastes and odors.

Ingredients that are moisture sensitive or hygroscopic remain challenges to encapsulation. With plant-based HPMC capsules, however, there are more opportunities than ever to address these challenges. HPMC capsules have significantly lower moisture content than gelatin and can be used in combination with desiccant materials with fewer concerns. Additionally, products that are very light or fluffy (such as red raspberry leaf powder) can be a challenge. These products need to be “densified” in order to flow and “pack” in the capsule better.

**Udell:** Softgels are challenging to work with because water-soluble/hydrophilic materials cannot be easily encapsulated. This can be problematic because the vast majority of nutrients are water soluble. The gelatin capsule itself is compromised when the water-loving properties of most nutrients leach into the capsule. For this reason, materials that are lipophilic tend to work better in the softgel delivery system, so you often see oils being encapsulated.

However, a high-end softgel encapsulator with an excellent R&D staff can often solve problems with hydrophilic materials. This is done by creating fine paste suspensions that involve a mixture of paste powders suspended in carrier oils. Suspensions enable hydrophilic nutrients to be encapsulated into soft gelatin capsules. It’s a fine balancing act between powder and liquid in the softgel.

**Israel:** Enhanced absorption CoQ10 (ubiquinone) has long been delivered in soft gel capsules. This delivery technology has been proven to provide enhanced absorption of this important nutraceutical over traditional two piece capsules. Traditional CoQ10 must be converted into ubiquinol for it to be “active” in tissue. Currently, a new form of CoQ10, a reduced form called ubiquinol, has been introduced to the industry by Kaneka, the leading manufacturer of CoQ10. Ubiquinol is exceptionally difficult to manufacture into finished dosage form, requiring exacting control of all stages of the production process. If not manufactured correctly, ubiquinol will rapidly deteriorate through oxidation into ubiquinone, the traditional form of CoQ10.

**INSIDER: How popular are controlled-release encapsulation technologies, and how is the demand driving innovation in encapsulation?**

**Udell:** In the past, controlled-release softgels were primarily only available through the addition of an enteric coating, which bypasses dissolution in the stomach and delays the release of the nutrient(s) until the product reaches the intestinal tract. Now there are many other ways to make controlled-release products more functional and allow them to enter the body at different sections of the gastrointestinal (GI) tract. One such way is through micro-encapsulation of ingredients with different materials that function in a similar way as enteric coating. This allows for individual ingredients to be delayed in release, rather than the entire formula. There are various matrices for the ingredients that will also speed up or increase bioavailability, and there are methods for prolonging the blood level of some ingredients. We have not received customer requests for these types of delivery technologies thus far, with the exception of enhanced bioavailability products.

**Israel:** Specialty ingredients and nutraceuticals are an area where controlled release technology will prove useful. Enteric coating of some unpleasant tasting or acid fragile ingredients has proven beneficial. The effectiveness and palatability of high quality marine lipid concentrates and probiotics will clearly benefit from these technologies. Robinson Pharma recently added a continuous process enteric coater (not the traditional batch process equipment) to allow for the addition of this value-added feature.