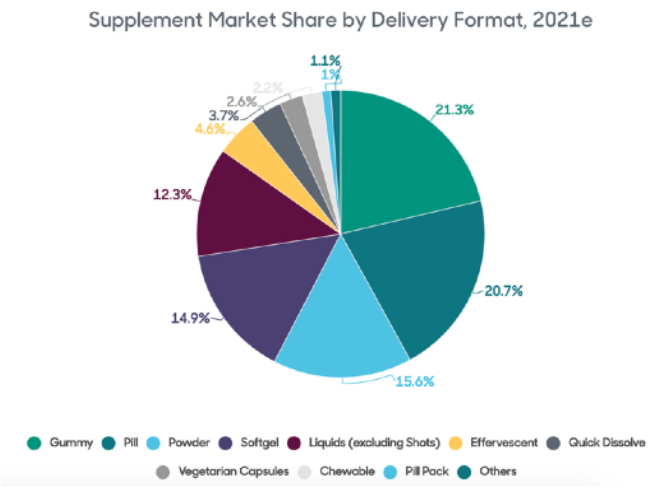
The Promise of Gummies as a Drug Delivery System

Looking at the supplement industry as a barometer for drug delivery systems, it's apparent that gummies are gaining traction as a preferred delivery system. In 2019, the sales of non-pill formats, including gummies, powders and shots, exceeded the sales of pill formats and that gap between the pill and non-pill market share continues to grow.

In 2021, non-pill delivery formats represented 60.8% of sales. Gummies are now the single largest format by market share (although the total for combined pills, softgels, capsules and pill



Source: Nutrition Business Journal

packs is still greater), and represent $12.97 billion in annual sales. The popularity of gummies is expected to grow as, according to Nutrition Business Journal, supplement consumers in 2021 chose non-pill formats for 60% of their purchases while the demand for tablets and capsules are flat to down and soft gels, on the supplement side, are also flat.

According to MarketsandMarkets, the global gummy vitamin market size is projected to reach $10.6 billion by 2025, recording a CAGR over 12%. The greatest barrier to achieving that growth? Lack of capacity.

To help meet the increasing demand for gummies and to explore the possibility of leveraging this growing market's delivery system beyond nutritional supplements, Avéma Pharma Solutions and its parent company, PL Developments, has invested in a new pharmaceutical quality manufacturing facility in New York, has set up a world class bench top lab in our Miami R&D center to help facilitate rapid gummy development and have added staff with gummy development experience to help drive the initiative.

The Challenges to Moving Beyond Supplements: Dosage, Production and Taste

Given the increasing demand for gummies in the supplement market, there has been significant interest in developing gummies that can deliver OTC and Rx drugs as well. Pharmaceutical companies see gummies as an ideal solution for the pediatric and geriatric markets where the population has difficulty swallowing pills and even softgels. Kids have also shown resistance to taking liquid medications – which often have an unpleasant flavor, so the ability have a chewable delivery system (i.e., gummy) is a huge benefit – providing it contains the right dosage, tastes good and has a great mouth feel.

For nutritional supplements, gummies are a natural choice because the exact dosage in each gummy may not be critical. That changes when companies look at OTC or Rx drugs, where the most important factor is dose accuracy. Consumers need to be confident, for example, that two acetaminophen gummies would be the equivalent of two tablets of acetaminophen.

To achieve the required level of consistency in the dosage form, it depends on the formulation process and the ability to work with different APIs. One of the advantages that Avéma Pharma Solutions brings to the table is that, as a division of PL Developments, the company has been developing delivery systems

for a broad base of formulations for more than 30 years, so we probably have experience with the actives already in another matrix, whether it be tablet, capsule, softgel, or liquid and can leverage this experience in the development of a gummy.

At Avéma's R&D Center, our team has experience with developing formulations as well as method development and validation.

The intimate knowledge of how to get your actives or your dietary supplements to interact correctly with the blend is key. At Avéma/PLD, a great part of our success lies in the fact that not only does the company have our own R&D center, we have the scientists on staff who can develop or modify formulations, test for actives and support method development/validation. That infrastructure is a massive benefit to the organization. The intimate knowledge of how to get your actives or your dietary supplements to interact correctly with the blend is critical to making successful gummies.

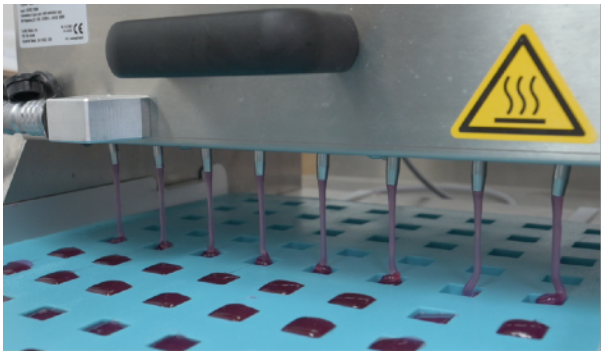
One of the challenges in producing gummies for drug delivery is that since most of the manufacturers of gummies are confectionary sites, they are not set up to make drugs, and many of the manufacturers that make drugs have no idea how to make gummies. It takes experience on both sides of the equation and the ability to marry these two skill sets together. When PLD purchased a world-class GDUFA-approved, pharmaceutical grade confectionary facility this gave us the springboard to formulate and manufacture novel, great tasting, functional gummies.

There are two ways to manufacture gummies – a starch-based process, mostly used for confectionary applications, and a starchless process. When using a starch-based system, typically manufacturers use a starch mogul: after filling a tray with cornstarch, the desired shape is stamped into the starch and then the cooked slurry is deposited into the holes left by the stamp. The entire tray is left to dry, typically for about 24 hours. The following day, the tray is inverted onto a screen. The powdered starch falls away and the gummies are left. The problems with this method include the long drying time and the possibility of cross contamination, either during the drying process or when the starch is reconditioned and reused.

Avéma's starchless manufacturing process eliminates issues with cross contamination.

To ensure the consistency, accuracy and purity of our gummies, Avéma uses a starchless production process. In this manufacturing technique, instead of depositing the cooked slurry into a stamped, powdered starch, it's deposited into a fixed mold where a chemical reaction in the formulation causes the gummy to solidify immediately. This allows the gummy to be quickly released from the mold so it can be dried in a separate room, freeing up the line to run a different product without fear of contamination.

At the PLD/Avéma facility, the physical infrastructure allows us to manage production at a level beyond what is mostly seen in this industry. The facility we operate is built to control – and therefore, eliminate -- cross-contamination. There are individual suites for every one of the lines and individual drying rooms for every batch. There are never products co-mingling in one large drying suite. In fact, we have an extra drying room that can accommodate a product that needs additional drying, enabling us to keep each line up and operating.



Bench testing and pilot manufacturing is done at Avéma's R&D Center.

There are a lot of critical parameters that need to be met in a starchless, gummy manufacturing environment in order to deliver a superior gummy, such as consistency in the liquid slurry, and the ability for the formulation to react and solidify once it's deposited. The initial formulation work for each product is done at Avéma's Miami R&D facility where our scientists work closely with the lab on the consistency of the product, the liquidity of the slurry, the active levels in the product, the pH of the product, and other critical parameters. Given the company's experience working with actives in a variety of solid dosage forms, the team has an advantage in being able to control actives within a gummy matrix. Once bench testing and lab scale manufacturing is complete, we then take it to a pilot scale test line in New York.

In terms of integrating actives, as a basic rule of thumb, we don't like to exceed 10 to 15% of the weight of the product inactive. So, if a typical gummy is two and a half to three grams, it would include approximately 250 to 300 milligrams of actives. The reason for not incorporating a higher level of actives would be to not adversely impact taste and also to ensure the formulation's ability to react and solidify once it's deposited. If the dose is at too high a level, the liquid slurry could be too thick. This could cause problems with depositing the slurry into the molds and cooling appropriately. One potential issue is that the outside of the gummy will develop a skin, which would make the gummy solid on the outside but gooey inside, rather than drying to an even consistency from the outside layer all the way through the gummy.

Once the formulation is developed, the next step is flavor masking and mouth feel. This is another area where Avéma's R&D capabilities are very helpful. Actives have different flavors, some are sweet, some are sour, some are bitter. Avéma has experience with masking flavors using a combination of sweeteners and flavors to mask the bitter or unpleasant taste of an API or even encapsulating actives using coated bead technologies, which can encapsulate the active in the gummy matrix until it is digested.

It's those three things working in concert with each other that are the key to making this all work, and this requires the right equipment, the knowledge of drug development and experience making gummies.

Regulatory Approvals

The final piece of the puzzle for developing gummies for OTC or Rx drugs is the regulatory aspect. In this area, having the experience baked in at PLD and Avéma is a key advantage as our team is experienced at working with the US Food and Drug Administration (FDA) on new drug applications (NDAs), abbreviated new drug applications (ANDAs) and more. No confectionary manufacturers and few supplement manufacturers can have a meaningful conversation around the development of a novel delivery system for a drug. At Avéma, we can show what has been done from a formulation standpoint, a stability standpoint, and a process control standpoint. We even have packaging capabilities, which will come into play when developing products that taste too good -- this would involve using child resistant packaging such as CRCs and child resistant blister cards.

Avéma Pharma Solutions and PL Developments have married confectionary expertise with not just supplement expertise, but a step above that, with the Rx and the OTC expertise that can help bring your nutritional supplement or drug to market. Currently, we have four production lines set up with a combined capacity of 1.2 billion gummies annually and are ready to help develop and manufacture your nutritional supplement or drug product.

Mitchell Slade is Chief Operating Officer at PL Developments, and President of the PLD Gummy co. Prior to joining PLD, Slade held various product development and operational roles for the Nature's Bounty Company, where he led a team to acquire and convert an existing candy factory to become a cGMP compliant nutritional gummy plant, capable of large scale nutritional gummy production.

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