NUTRACEUTICALS

The Challenges and Opportunities of Complex Nutraceutical Products

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The global nutraceuticals market was estimated at $317.22 billion in 2023 with a projected CAGR of 9.6% from 2024 to 2030.[1] The key drivers for this growth are preventive health care, growing awareness of health maintenance, metabolic disorders such as obesity, diabetes and cardiovascular disease, and increased consumer interest in wellness and personalized nutrition.

Manufacturers have responded to the growing demand for nutraceuticals by introducing novel, complex formulations that not only increase market appeal of products but also improve therapeutic efficacy and safety. New technologies such as controlled release and patient-centric formulations allow manufacturers to create sophisticated formulations that enhance bioavailability and target specific health needs. These technologies not only improve the efficacy of nutraceuticals but also allow for tailored solutions that cater to individual consumer requirements.

As the market continues to evolve, the integration of these advanced approaches will enable manufacturers to overcome challenges in the development of new formulations, playing a crucial role in shaping the future of nutraceuticals.

Defining Nutraceuticals

A nutraceutical is a product derived from food sources with extra health benefits in addition to the basic nutritional value found in foods. The term 'nutraceutical' combines 'nutrition' and 'pharmaceutical,' indicating its dual role in providing nourishment and medicinal benefits.[2]

Nutraceuticals include a wide range of products such as isolated nutrients, dietary supplements, herbal products, specific diets, and processed foods like cereals, soups and beverages. Nutraceuticals are often used to:

- Prevent chronic diseases
- Improve health
- Delay the aging process
- Support the structure or function of the body

Despite their widespread use and recognized benefits, nutraceuticals don't have a standardized regulatory definition. This ambiguity can lead to confusion among consumers and within the industry. For instance, a nutraceutical may be considered a food in one country and a drug in another, affecting its marketability and regulatory compliance.

Benefits of Complex Formulations

Modified release (MR) dosage forms are designed to control the rate and location in which ingredients are delivered. Complex nutraceuticals with advanced MR offer several key benefits:

- **Sustained nutrient delivery:** Slow-release formulations provide a steady supply of nutrients over an extended period, rather than a rapid spike followed by a drop-off. This allows for more consistent absorption and utilization by the body.
- **Improved bioavailability:** Controlled release systems can enhance the bioavailability of nutrients by protecting them from degradation in the stomach and releasing them in optimal absorption sites in the intestines. This is especially beneficial for compounds sensitive to stomach acid.
- **Targeted release:** Enteric coatings and other technologies allow for targeted delivery of ingredients in specific areas of the gastrointestinal tract, bypassing stomach acid degradation.
- **Enhanced stability:** Advanced formulations and packaging solutions can protect sensitive compounds from degradation due to light, heat or moisture, extending shelf life.
- **Convenience and compliance:** Slow-release formulations may allow for less frequent dosing, improving consumer compliance and convenience.
- **Product differentiation:** These technologies allow companies to create unique formulations and line extensions of existing products.
- **Improved efficacy:** By optimizing absorption and utilization, these formulations may provide greater health benefits compared to traditional supplements.
- **Consumer preference:** Many consumers perceive advanced delivery systems as more sophisticated and effective, potentially increasing product appeal.

These innovative solutions to complex formulations can help overcome challenges in the development of nutraceuticals. However, it's important to note that while these technologies offer potential benefits, their effectiveness can vary depending on the specific nutrients and formulations involved. Additionally, time-release supplements may not always provide superior results compared to traditional formulations for all nutrients. The choice between complex and conventional (immediate release) nutraceuticals should be based on scientific evidence of efficacy and individual health needs.

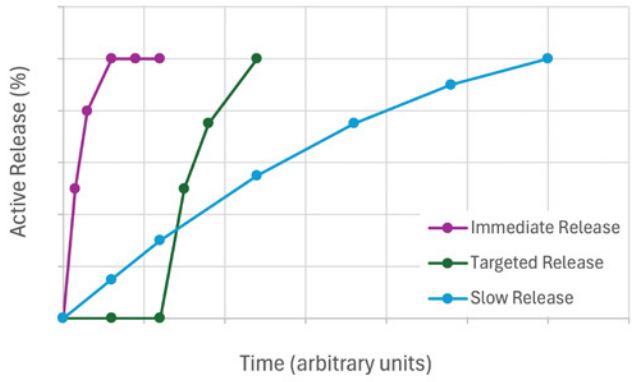


Figure 1

Modifying the release of active nutritional ingredients

NAI Formulation Challenges

Formulating nutritional active ingredients (NAIs) into effective and consumer-friendly products presents several challenges. Here are some key issues:

1. Flowability and Compressibility

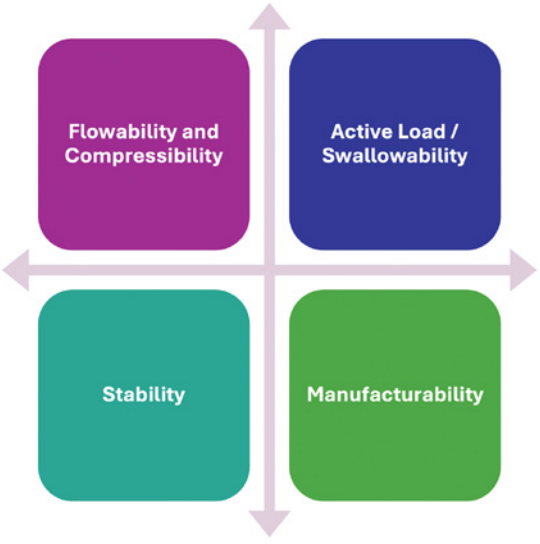
Ensuring that NAIs flow smoothly through manufacturing equipment is essential for consistent dosing and product quality. Poor flowability can lead to clogging, inconsistent tablet weights, and uneven distribution of active ingredients. NAIs must be able to be compressed into tablets without breaking apart or losing efficacy. Poor compressibility can result in weak or friable tablets that disintegrate during packaging, shipping or handling.

2. Active Load/Swallowability

Incorporating a high concentration of NAIs into a single dosage form can be challenging. High active loads may affect the physical properties of the formulation, making it difficult to process and potentially impacting the stability and bioavailability of the active ingredients.

Additionally, formulators must carefully balance the amount of active ingredients with excipients (inactive ingredients) to ensure the product is effective, stable and manufacturable.

High active loads can also impact the size of the finished product. This can present a challenge in the formulation of nutraceuticals and dietary supplements that are suitable dosage forms for different groups or aging populations, especially older adults and children that have limitations in swallowing (dysphagia). As such, dosage forms such as orally disintegrating tablets, microencapsulated powders (taste masked), gummies and easy swallow film-coated tablets should be considered.



3. Stability

Many NAIs are hygroscopic, meaning they absorb moisture from the environment, which can lead to degradation or reduced efficacy. Formulating these ingredients requires protective measures such as microencapsulation of the NAIs, moisture-resistant packaging, or the inclusion of desiccants or moisture barrier film coatings.

Certain NAIs are prone to oxidation, which can compromise their effectiveness. Antioxidants or protective coatings may be necessary to preserve the integrity of these ingredients. Some NAIs degrade at elevated temperatures, necessitating controlled manufacturing environments and storage conditions. This is a key challenge when manufacturing gummies and technologies such as microencapsulation will need to be considered.

4. Manufacturability

Formulations that work well in small-scale laboratory settings may encounter issues when scaled up to commercial production. Consistency in mixing, granulation and tablet compression must be maintained. The formulation must be compatible with existing manufacturing equipment to avoid the need for costly modifications or new machinery. The formulation process must be cost-effective, balancing the use of high-quality ingredients with the need to keep production costs manageable.

Achieving Targeted Therapy Goals and Functionality

In the pursuit of targeted therapy goals and enhanced functionality, nutraceutical manufacturers are looking to solutions for more complex product formulations. These solutions can address key challenges, such as stability, palatability, targeted release kinetics and manufacturability.

Enhanced stability techniques ensure that active ingredients maintain their potency throughout the product's shelf life, while innovative taste-masking methods transform traditionally unpalatable compounds into consumer-friendly products.

To achieve more complex therapeutic goals, formulators may employ combinations of various modified release technologies to enable unique delivery patterns. Delayed release (DR) technologies may be used when NAI degradation occurs (in probiotics for example) due to stomach acidity.

Many NAIs have a short half-life, so extended-release formulations may provide improved therapeutic outcomes and reduce dosing frequency. For example, exogenous administered forms of melatonin are marketed as improving sleep duration and may help patients who awaken intermittently or too early. The use of polymeric matrices to formulate a melatonin tablet can provide a combination of fast onset of drowsiness and extended release to improve sleep duration and avoid morning drowsiness. Multiparticulate (pellet) dosage forms allow a combination of NAIs that may be incompatible in a single monolithic tablet. They also allow combinations of immediate, delayed and extended-release pellets in the same dosage form to achieve targeted release profiles.

This synergy of technological innovations not only elevates the efficacy of nutraceuticals but also paves the way for personalized solutions, ultimately bridging the gap between conventional supplements and more complex nutraceuticals.

Key Takeaways

The nutraceutical industry is poised for significant growth, driven by consumers' demand, advancements in technology and the availability of complex formulations that enable the development of patient-centric products. With innovations such as controlled release and patient centric formulations,

manufacturers can create sophisticated formulations that enhance bioavailability and target specific health needs. The integration of these advanced approaches will play a crucial role in shaping the future of nutraceuticals, ultimately leading to more effective and accessible health solutions for consumers.

References

1. Nutraceuticals Market Size, Share & Trends Analysis Report by Product (Dietary Supplements, Functional Foods, Functional Beverages). Grand View Research.
2. Puri, V, et. al. A Comprehensive Review on Nutraceuticals: Therapy Support and Formulation Challenges. Nutrients. Nov. 2022.

About the Authors

Charles Vesey, RPh, MS *serves as the Senior Formulation Technology Manager at Colorcon. In this role, he oversees the technical aspects of Colorcon's Formulation Technology business in North America, focusing on solid oral dose and modified release design and development. With over 25 years of experience in pharmaceutical development, Chuck is recognized as a thought leader in pharmaceutical formulation and process troubleshooting, particularly for multiparticulate controlled-release products. He holds both a Bachelor's in Pharmacy and a Master's in Pharmaceutics from the Philadelphia College of Pharmacy. Chuck is a member of the American Pharmacists Association, a licensed pharmacist in Pennsylvania, and a United States Pharmacopeia Expert Committee Member.*

Sandeep Kumar, Ph.D. *is the Formulation Development Manager at Colorcon, where he specializes in creating innovative pharmaceutical and label-friendly nutraceutical solutions. With extensive experience at leading organizations like Thermo Fisher Scientific and Catalent Pharma Solutions, Dr. Kumar is an expert in developing cutting-edge solid dosage forms, including tablets and capsules. At Colorcon, he plays a pivotal role in supporting the nutraceutical industry with products like Nutracore, a range of natural excipients designed to meet clean-label demands while ensuring superior manufacturability and performance. His work empowers manufacturers to deliver sustainable, high-quality products that align with consumer preferences for transparency and natural ingredients.*

Capsules & Capsule Equipment

Sorbent Capsules for Moisture Control

Colorcon's EQIUS® Equilibrium Relative Humidity Stabilizers provide precise moisture control, maintaining a specific relative humidity (RH) range of 10%-95% within pharmaceutical and nutraceutical packaging. They effectively manage both overly humid and overly dry conditions. For instance, the APIs inside hard gelatin capsules can be susceptible to hydrolysis when conditions exceed a certain RH level, while the capsule itself can become brittle with excessive dryness. Additional applications include capsules for drug powder inhalers and gummies. EQIUS are available in various configurations compatible with standard insertion and packaging equipment including canisters, packets, closures and bags for bulk applications.

Colorcon, www.colorcon.com

Capsule Filling for Probiotics

IMA Active's Practica is the ideal choice for probiotic encapsulation thanks to its advanced dosing technology. One of the most important factors for probiotics is to keep the product alive after it enters the capsule. To achieve this, Practica ensures gentle handling, preserving probiotic viability with minimal thermal impact. It also guarantees precise dosing, weight consistency and ease of use, allowing for simple weight adjustment without changing dosing plates. The machine's intuitive design and quick assembly and disassembly make it an efficient and reliable solution for the dietary supplement industry.

IMA Active, www.ima.it

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JC-Caps® brand Bright-Poly capsules are the world's first USDA National Organic Program (NOP) certified organic vegetable capsules. The capsule wall structure is made with USDA NOP certified pullulan using self-developed technologies and formulation, without using NOP prohibited ingredients, such as sodium lauryl sulfate (SLS) or salts of fatty acids. Pullulan film is almost 10 times better than gelatin film and HPMC film in blocking oxygen penetration. Bright-Poly capsules are naturally derived and environmentally friendly, as the pullulan is extracted from fungi using water. The capsules maintain machine-ability, free flow and clear visual appeal.

Bright Caps GmbH, www.brightcaps.eu

Efficient Capsule Polishing

Krämer KCP series of capsule polishers feature highly efficient capsule polishing with conveying heights of 800 mm to 2000 mm in a very small footprint. Units offer the integration of a capsule polisher, metal detector (Ceia, Loma/Lock and Safeline) and diverter/empty capsule sorter in one base. All polishers are made to the latest CGMP standards and are easy to assemble and disassemble for cleaning without tools due to their modular structure.

Krämer, www.kraemerag.ch