Lonza

Capsules & Health Ingredients

Challenges and Solutions in Formulating Probiotics

Formulation Challenges

How to protect and deliver probiotics, living cells sensitive to environmental conditions

HUMIDITY AND TEMPERATURE

Probiotics are sensitive to moisture intake and temperature during transportation.

One of the major sources of probiotic degradation is water. Several sources of water can be identified during the manufacturing process.

PROTECTION FROM STOMACH ACIDITY

Probiotic strains can be sensitive to acidic environments.

The main source of probiotic degradation is exposure time to stomach acidity after ingestion.

EXPECTATIONS OF POTENCY

Consumers expect that the amount of probiotic indicated on the labeling will actually be delivered in their body.

CONSUMER EXPECTATIONS

75%

Three-Fourths of consumers prefer vegetarian capsules

54%

Over half of consumers look for science-based evidence

Source: NMI SORD US-EMEA Consumer Trends & Insights Report 2019

Lonza's Innovative Dosage Form Solutions Portfolio for Probiotics

Three Solutions to address main probiotic formulation challenges

DOSAGE FORM SOLUTION OPTIONS

DRcaps®
capsules

Protection from stomach acid allowing for delayed delivery

Vcaps®
Low moisture capsules

Protection from humidity

DUOCAP®
capsules

Consumer expectations - product combination

Vcaps® hypromellose capsules

Increase the stability of hygroscopic sensitive actives like probiotics

Vcaps®

ADDRESS HUMIDITY TO PRESERVE PROBITIC STABILITY AND VIABILITY

CAPSULE POLYMER

Vcaps® capsules
Composed of HPMC and a gelling agent. Slightly delayed dissolution at pH 1.2 vs hard gelatin capsules

STABILITY

These low moisture capsules have been produced under specific conditions, and they are packaged in aluminum bags to ensure lower moisture content for 12 months if left unopened and stored under standard storage conditions.

FILLING PROCESS

Relative humidity (RH) must be controlled throughout the complete manufacturing process when filling low moisture capsules. The conditions should be monitored and kept below 30% RH.

MACHINABILITY

Tested on major capsule filling machines and preserve mechanical properties at as low as 2.5 % water content.

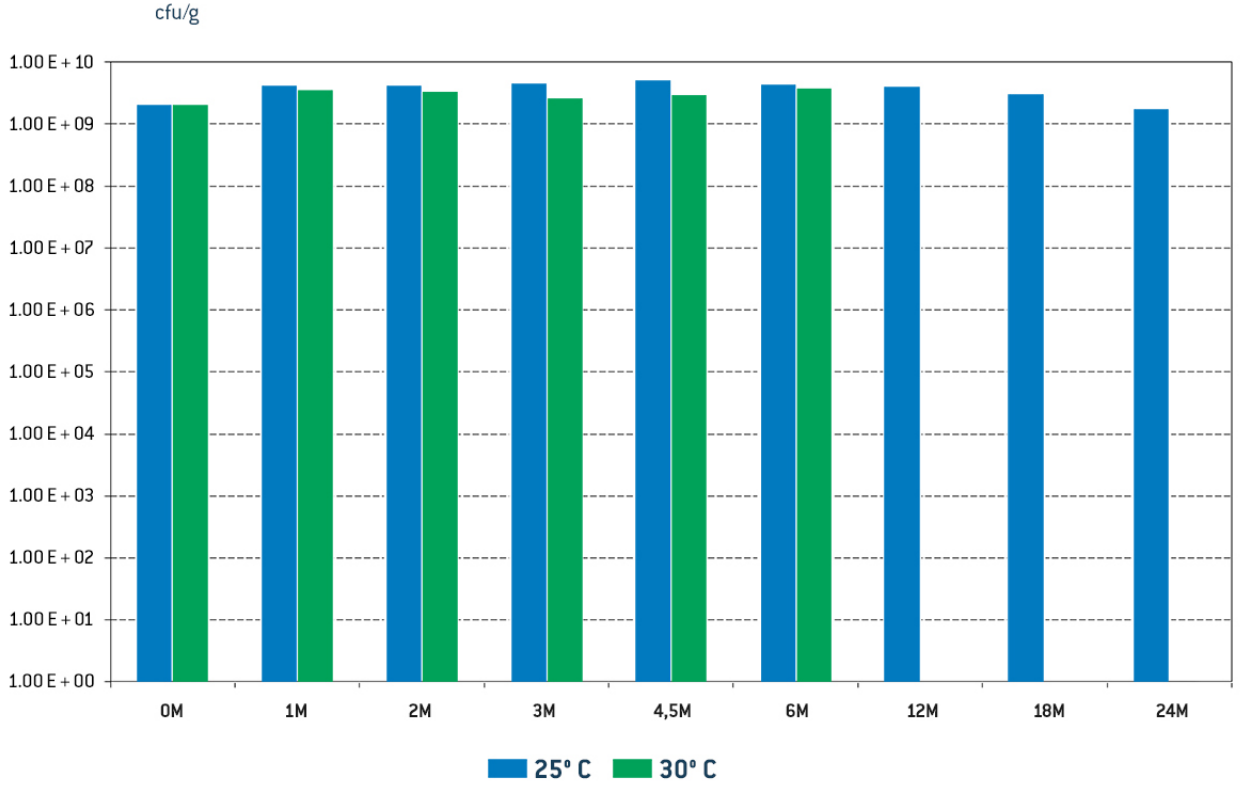
Vcaps® hypromellose capsules provide enhanced stability of probiotics

Lactobacillus A. and Bifido B. strains experience improved stability compared to traditional gelatin

Capsules were filled with a mix of Lactobacillus A. and a Bifido B. and stored in tube with desiccant at 30°C / 65%RH and 25°C / 60%RH

High stability observed with Low Moisture Vcaps® hypromellose capsules up to **24 months** minimum

Probiotic stability in Vcaps® packaged in aluminum tube with desiccant



Stability study, Capsugel, 2015

DRcaps® capsule

Protection from stomach acidity

DRcaps® hypromellose capsules

WINNER nbt NUTRACEUTICAL BUSINESS & TECHNOLOGY AWARDS 2013

DRcaps® plant–based designed release capsules

Why DRcaps® capsules for your probiotics?

- Increases shelf Life
- Protects from stomach acidity
- Supports clean label trend
- Enhances consumer experience
- Helps innovation

DRcaps® Capsules Contribute to Probiotics Stability

Plant-based Hypromellose Capsule Protects Against Moisture

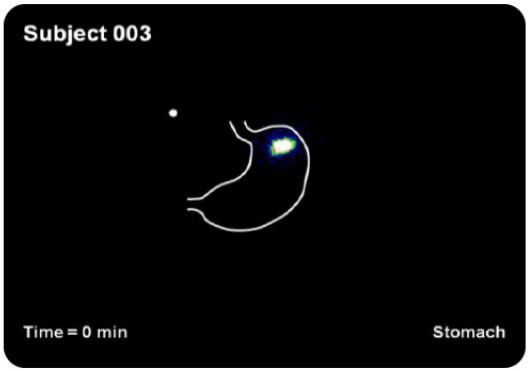
- Hypromellose capsules are also available as DRcaps® Low Moisture capsules
- No cross-linking activity with the capsule shell
- Hypromellose capsule resistant to temperature
- No additional treatment of the probiotic filling (e.g. tablet compression)
- Low brittleness capsule suitable for high-speed filling equipment

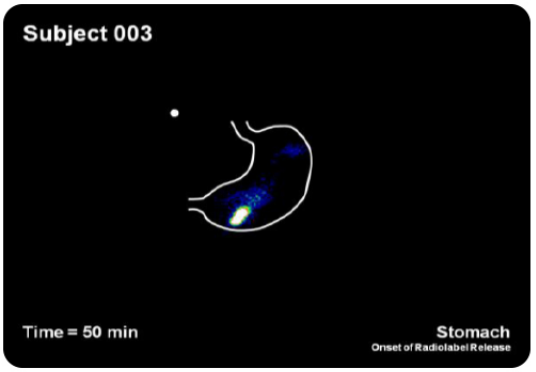
DRcaps® – Clinically studied and proven

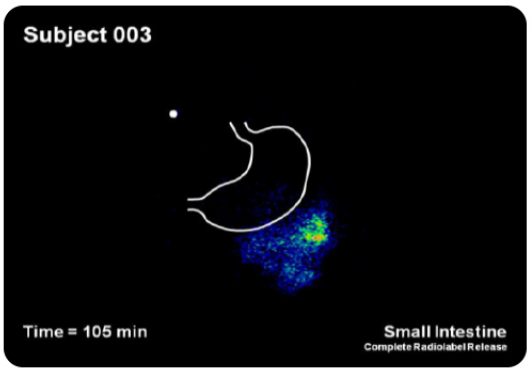
Dissolution test confirms acid resistant effectiveness of DRcaps®

Key Study Findings:

- DRcaps® capsules displayed delayed-release properties
- Disintegration started approximately 52 minutes after ingestion
- For the majority of subjects, complete release took place in the intestine
- Complete release occurred 20 minutes after the onset of release







Source: DRcaps® Human Clinical Study

DRcaps® Capsules Enhance Consumer Convenience

Easy to swallow reduced aftertaste dosage form

Convenience is a top priority for US consumers. In fact, at least 86% of those surveyed listed the top three features of usability for dietary supplements to be:

- Easy to digest / easy on stomach
- Easy to swallow
- Available in an easy to use / consumer format

DRcaps® Human Clinical Study

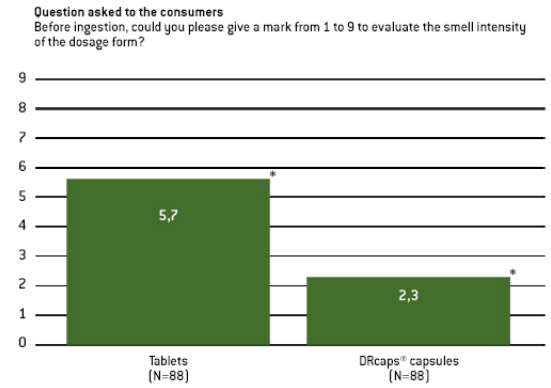


Figure 1: The perception of the smell intensity of the dosage form by the consumers

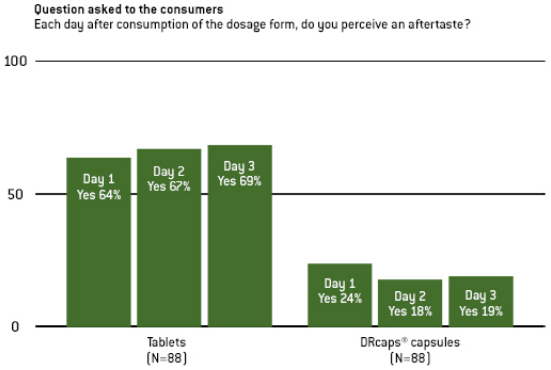


Figure 2: The aftertaste perception of the dosage form by the consumers

DRcaps® Capsules

Supports clean label trend

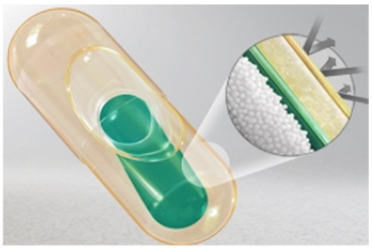
- Consists of only hypromellose, gellan gum & water
- Plant-based origin from sustainably sourced pine trees
- Non-GMO
- Compatible with vegetarian / vegan diet
- Halal & Kosher
- No allergens or preservatives
- Allows clean label claims expected by the consumer
- Eliminates the use of chemical coating
- Allows responsible use of ingredients

DUOCAP® Capsule

Improve stability and facilitate delayed release

DUOCAP® capsule–in–capsule technology for probiotics

Combine protection against moisture, designed delivery and innovative formulations



- Perfect for moisture-sensitive compounds: Glycerol in external capsule prevents water absorption in internal capsule.
- Internal capsule can be DRcaps®, Vcaps®, or Vcaps® Plus for wide-ranging solutions.
- Liquid-filled vegetarian plant-based dosage form.
- DUOCAP ® capsules can contribute to the stability of probiotics.
- Allows for a second ingredient in the outer capsules to expand structure function claims (e.g. Vitamin D).
- Ideal for one capsule, once a day treatments.

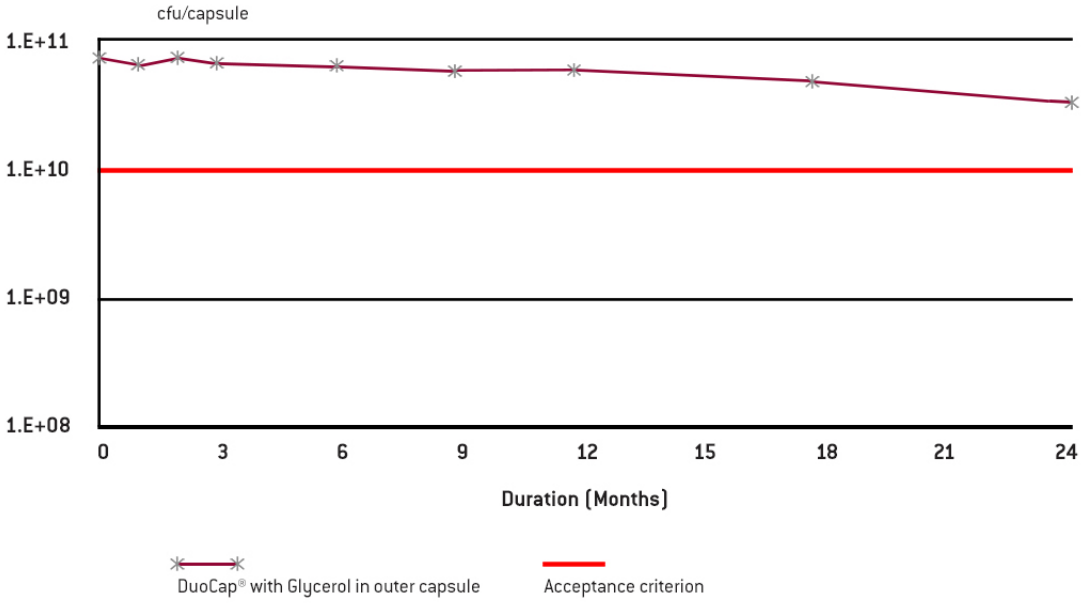
DUOCAP® design to support probiotic stability

Allows for probiotic powder in liquid-filled combination products

Inner capsule - Vcaps® size 3
Filled with 100% probiotic

Outer capsule - Vcaps®
size 00 containing glycerol

Probiotic stability in DUOCAP® capsules filled in PP bottle stored for 24M at 25°C/60% RH



Storage conditions:

- 4-8°C and 25°C / 60% RH

Storage conditions	T0	T 1M	T 2M	T 3M	T 6M	T 9M	T 12M	T 18M	T 24M	T 36M
4-8°C	X	X		X		X	X	X	X	X
25°C 60% RH		X	X	X	X	X	X	X	X	X

Conclusion: Stability Study confirmed stability of probiotic in DUOCAP®

Stability study, Capsugel 2015

Our Dosage Form Solutions for Probiotics

In the extremely competitive probiotic landscape, creating a stable and efficient delivery system is critical to retaining a loyal customer base. Putting product performance at the heart of communications can also help brands win more consumers, and even extend into new markets and applications.

As a global leader in deliverying high-quality, innovative dosage forms and solutions, Lonza CHI brings the formulation answers you need to achieve commercial success. For over a decade we have been working to overcome the traditional challenges associated with formulating probiotic products.

Would you like to learn more about how Lonza can help you to meet your technical or marketing goals? Choose from the challenges below and discover which product will give the desired functionality.

Challenges	Solution	How can we help?
Achieve maximum shelf life	Improve stability by decreasing capsule water content, to create optimal conditions.	DRcaps®, Vcaps® and Vcaps® Plus HPMC capsules help to protect ingredients that are sensitive to moisture. DRcaps® Vcaps® Vcaps® Plus
Increase strain survival and delivery efficiency	Select a dosage form with proven stomach acid resistance, to ensure the delivery of probiotics into the intestine.	DRcaps® capsules safeguard probiotics in the passage through the stomach, without the cost and complexity of enteric coating. DRcaps®
Meet the specific needs of children and consumers with swallowing difficulties	Enable probiotics to be orally administered by simply sprinkling the contents into soft food, with easy-to-open capsules.	Coni-Snap® sprinkle capsules are an alternative to sticks and sachets and can be filled on the same machines as traditional capsules. Coni-Snap® sprinkle easy open capsules
Create combination products with EFSA claims	Stand out in a competitive market and deliver probiotics with other actives in 2-in-1 capsules.	Our DUOCAP® patented capsule-in-capsule delivery system allows for the effective delivery of probiotics and is ideally suited for combination or dual-release products.
Explore alternative delivery routes	Target the growing market for women's health products, with innovative dosage formats including vaginal delivery capsules.	With Vcaps® Plus HPMC capsules, you can benefit from added protection and rapid dissolution advantages. Vcaps® Plus
Cater to rising demand for clean label supplements	Choose delivery forms that facilitate your label claims, to appeal to the latest consumer preferences.	Our portfolio of vegetarian capsules delivers optimal performance for the manufacturing of safe and effective clean label food supplements.

Lonza's low moisture **Vcaps®** and **DRcaps®** plant-based capsule dosage forms meet the imperatives of successful formulating of probiotics.

DRcaps® capsules helps to protect sensitive probiotics against stomach acid, while delivering into the intestine.

DUOCAP® technology not only allows protection against moisture but also allows the creation of novel probiotic applications.

Contacts:

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