Challenges in the Development and Stability of Probiotic Formulations

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Probiotic Stability
Probiotics: parameters influencing their stability

Probiotics have to pass two main hurdles:

- Stability over shelf life
- Efficient delivery in appropriate site in the GI tract

Parameters influencing above:

- Humidity
- Temperature
- Pressure during manufacturing
- Acid stomach conditions
Probiotics consumption is mainly in food product (yoghurt, drinks) and food industry (cheese, wine…).

But food supplement consumption is increasing in double digits for last 10 years and main dosage forms are:

- Capsules
- Sachet / Sticks
- Vials
- Tablets

Also exists in specific applications:
- Chewing tablets
- Dispersion in oil
- Vaginal capsules
Formulation parameters

Probiotic can be

- Liquid solution: mainly used in food industry
- Lyophilized powder: mainly used in supplements
- Encapsulated probiotic: can be used in supplements and food. However, encapsulation is not adapted to all probiotic strains and would increase cost

Excipient

- Should have low water activity (< 0.2)

Manufacturing

- Line with independent air treatment and controlled temperature (<20°C +/- 2°C) and < 30% RH.

We will concentrate in our presentation on formulation of food supplements based on lyophilized probiotic
Sachet / Sticks

**Formulation**
- Probiotic dose is in general in the range of 20-100mg
- Rest (up to few grams) is excipient (flavoring, filler…) or prebiotic

**Stability**
- Gentle filling conditions with high stability of probiotic

**Dosage form ingestion**
- Mainly dispersed in water before ingestion
- Some can be directly taken (mainly stick with low amount of powder / oro-dispersible)

**Delivery in GIT**
- Sticks are to be taken with meal to increase survival through stomach acid

**Manufacturing**
- Low / No stress on probiotic during filling
- Costly oral dosage form

**Consumer**
- Could be difficult to open for elderly
- Adapted for children
- Consumer prefers minimum excipient in formulas
Vials

Formulation
• Probiotic dose is in general in the range of 20-100mg
• Rest (up to few grams) is excipient (flavoring, filler…), prebiotic, nutrient...

Stability
• Water vapor pressure in bottle increases risk of destruction of probiotic powder in cap

Dosage form ingestion
• Cap is twisted, powder formula falls in liquid, is mixed and drank

Delivery in GIT
• Mix will go through the stomach acidic harsh conditions before arriving to intestine

Manufacturing
• Multiple step manufacturing not always available in house
• Costly oral dosage form

Consumer
• Could be difficult to open for elderly (twisting cap is hard)
• Adapted for children
• Consumer prefers minimum excipient in formulas
• Not easy to transport
Tablets

Formulation
• Probiotic dose is in general in the range of 20-100mg
• Some amount of excipient, increasing if tablet is coated or if other nutrients are added...

Stability
• Probiotic suffers from 2 main critical parameters: pressure and temperature build up.
• Coated tablet can be manufactured but this adds stress of coating solution and drying heat leading to increase of destruction of probiotic

Dosage form ingestion
• Easy to take with water

Delivery in GIT
• Tablet will open in stomach under acidic harsh conditions before arriving to intestine.
• Coated tablet will open in intestine

Manufacturing
• Multiple step manufacturing not always available in house (multilayer tablet, coating...)
• Higher than standard tablet cost and formula composition is complex (lower speed, less pressure...)
• Needs expensive packaging (Alu / Alu or tube with desiccant)

Consumer
• Easy to transport
• Could have some odor, taste and have high amount of excipients
Capsule: DRcaps® Acid resistant capsule

Formulation
• Probiotic is in general in the range of 20-100mg
• Little excipient needed (simple formulation, small capsule …)

Stability
• Gentle filling conditions with high stability of probiotic.
• Low water content in capsule permits a long shelf life

Dosage form ingestion
• Easy to take with water

Delivery in GIT
• Specific capsule which do not dissolve under gastric conditions permitting to delivers probiotic near or in intestine. The delay in opening was confirmed with a human in vivo scintigraphy study

Manufacturing
• One step easy formula to fill on standard hard capsule filling machine
• Packaging cost can be reduced as capsule has low water content and is mechanically stable even in presence of desiccant in package

Consumer
• Small capsule easy to take and transport with no odor or taste.
• Can be colored or printed to improve awareness and compliance of consumer
**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
Capsule: DuoCaps™

Dosage Form
• Innovative dosage form consisting of an interior capsule with probiotic and an exterior capsule filled with a liquid mixture. Different interior capsule types can be used including DRcaps®.

Formulation
• Probiotic is in general in the range of 20-100mg filled in the interior capsule.
• Liquid can be an oil or glycerol based containing actives with synergetic benefit.

Stability
• Gentle filling conditions with high stability of probiotic.
• Low water content in capsule permits a long shelf life.

Dosage form ingestion
• Easy to take with water.

Delivery in GIT
• Depending on interior capsule probiotic can be delivered throughout the GIT.

Manufacturing
• Two step process including sealing of capsules on a patented LEMS line.
• Packaging cost can be reduced as capsule has low water content and is mechanically stable even in presence of desiccant in package.

Consumer
• Small capsule easy to take and transport with no odor or taste.
Main dosage forms adapted to probiotics are: Sticks/ sachet and capsules

Although stability in both cases is high the final choice will be function of

- Total dosage weight
- Cost of goods
- Target patient population
- Patient compliance

Maturing probiotic market is looking for innovative dosage form and DRcaps®, a specific acid resistant capsule, has the potential to deliver probiotics in intestine permitting an increased efficiency of your formulation with a low development and manufacturing cost.
Thank You For Listening
Any Questions?

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