Lonza
Pharma & Biotech

tastemasking for enhanced oral delivery

The quest for more-effective tastemasking approaches has attracted significant interest because of the compelling effect tastemasking has on patient compliance, particularly among pediatric and geriatric patients. The challenge remains meeting diverse product specifications in a narrow formulation space. Lonza utilizes an array of specialized tastemasking technologies and formulation approaches to address the bitter taste of many APIs in an efficacious oral dosage form. We combine industry-leading expertise in innovative tastemasking approaches with enabling technologies used to create the optimal drug-delivery solution. We also offer a full range of specialized capsules, such as sprinkle-capsules, which provides additional tastemasking as well as dosing functionality and flexibility.

Effective tastemasking strategies

Tastemasking is typically accomplished in one of three ways.

- Using sweeteners, flavors and viscosity modifiers to manipulate the perception of taste without changing the concentration of free (unbound) drug in solution
- Preferentially binding the drug to a substrate that reduces the free-drug concentration, preferably below the taste threshold
- Applying functional coatings that modify the release of drug, keeping the free-drug concentration below the taste threshold for a time period relevant to the preparation and administration of the dose

Lonza uses all three of these approaches dependent upon application. In our experience, applying functional coatings is often the most effective.

During formulation, we utilize a risk-based approach to select excipients, evaluating precedented components with established safety data at levels that achieve the desired dosage-form performance and stability. Initial quality control metrics are the amount of active released over an appropriate time in a volume of medium or vehicle relevant to preparation and administration, and the amount of active released over an appropriate time in a medium relevant to the mouth.

Based on the initial characterization data and target product profile, the optimal tastemasking strategy and dosage form are selected. This may include multiple approaches – for example, lipid multiparticulates with functional coatings. We work to select a formulation that is stable, ideally preservative-free and amenable to flexible, uniform dosing across a broad patient platform.

We define the optimal technology based on specific API characteristics and target product profile to achieve tastemasking and modified release using coatings.

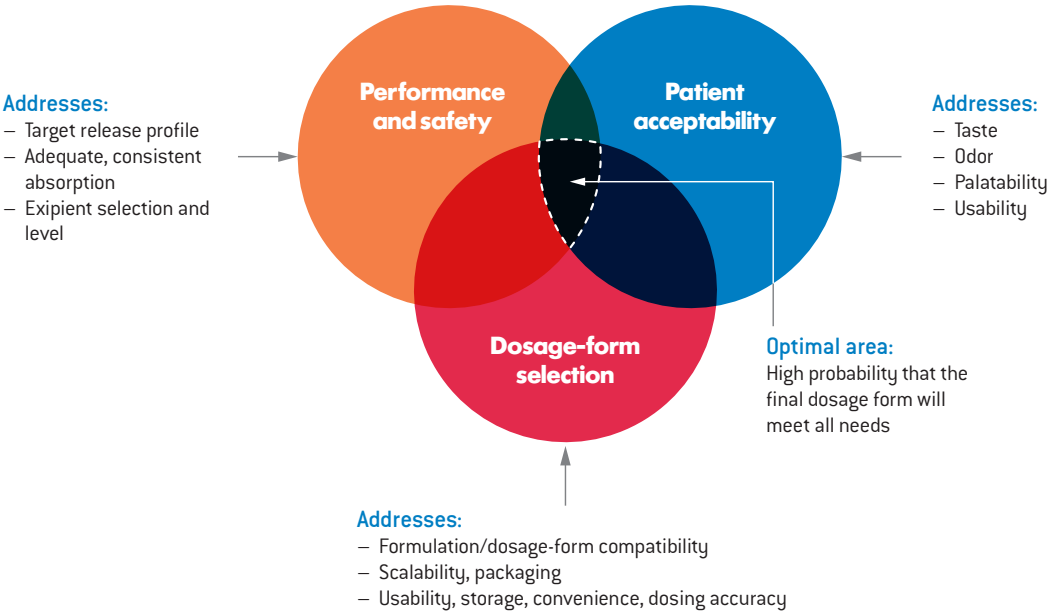
- pH-triggered (enteric, reverse enteric)
- Time-release (bursting)
- Diffusion-controlled (porous) or erosion-controlled formulations
- Lipid-based (LMPs)

Tastemasking for enhanced oral delivery

A fundamentals-based approach

Because palatability is dependent on multiple factors, including texture or mouth-feel, odor, taste and after-taste, we evaluate the need for tastemasking specifically as a first step. For example, we have found that multiparticulates below 250 microns in diameter typically have good mouthfeel for patients and can therefore facilitate palatability. Ideally, taste issues that may determine compliance risk for special populations are identified from sensory information early in clinical development.

A thorough characterization of the active ingredients is conducted in an initial screening process. We work closely with our clients to identify key components of the target product profile, addressing issues such as bioperformance equivalency with previous formulations, precedented excipients that are safe and suitable for use, and the ideal release profile for the target patient population.



Case study — lipid multiparticulates (LMPs)

We recently applied our expertise and technologies to the development of a tastemasked formulation for metastatic non-small-cell lung cancer carcinoma. Using well-established methodologies, Lonza worked with the client to develop a clear problem statement. The active compound, a small molecule with moderate aqueous solubility at physiologic pH, had a bitter taste. The goal was to develop an immediate-release formulation that masked the drug's bitterness and was bioequivalent to the existing solution formulation. Patient compliance was a key issue. The formulation components had to be acceptable for pediatric use, non-gritty, easy to swallow and have little taste, odor or aftertaste. Other criteria included ease of administration, accuracy of dosing, adequate shelf life and safety.

Our solution was an LMP sachet formulation. The particle cores were based on generally recognized as safe (GRAS) lipids, and the use of functional excipients (coatings, pore formers) was intentionally minimized. A reverse-enteric polymer was used for tastemasking and immediate release in the stomach. Particle size was controlled to 150 to 250 µm for optimal mouth feel. Based on palatability, safety and performance (*in vitro* dissolution) tests, a coating level of 20% was progressed through development and into clinical manufacture. The coated LMP product provides effective tastemasking and immediate release.

Learn more about how Lonza's tastemasking technologies can help you develop optimal drug delivery solutions.

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