EXPERT INTERVIEW

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TASTE MASKING 101: A Q&A WITH THE EXPERTS

The negative impacts of poor patient adherence, including harmful health outcomes, heightened medical intervention, and higher costs, represent an increasingly important consideration for drug manufacturers and regulators alike. While much of this equation is influenced by factors outside a pharmaceutical company's control, there are several taste masking strategies drug developers can implement to improve a drug's palatability, thereby increasing its potential for greater patient adherence, particularly for pediatric and geriatric populations.

Taste Masking 101 Optimize Taste and Improve Outcomes, the first of a four-part series hosted by Adare Pharma Solutions and International Flavors & Fragrances, Inc. (IFF), covers the industry challenges surrounding taste masking, including swallowability, palatability, efficacy, and patient accessibility. Drs. Luigi Boltri, senior director of pharmaceutical sciences at Adare, and Nasrin Mahmoudi, technical manager at IFF, discussed various taste masking strategies and the factors that influence different approaches, as well as the regulatory incentives to employing taste masking as part of an oral formulation. The pair emphasized the importance of patient acceptance and adherence as a consideration in drug formulation, outlining the ways in which taste masking can improve patient outcomes.

The following Q&A session was held after this webinar, in which Boltri and Mahmoudi addressed questions from attendees regarding the best practices, technologies, and strategies for incorporating taste masking in the formulation process.

What taste masking options are available for coating moisture-sensitive, bitter drugs?

Mahmoudi: We can use any conventional equipment for non-aqueous coating and solvent coating. We have multiple options: a fluid bed or a spray dryer for solvent coating, high shear granulation for applying lipid excipients, polymer coating, spray congealing, hot-melt extrusion, and other options for application of lipidic and thermoplastic polymers.

Polymers like ethylcellulose with thermoplastic properties and having a wide range of solubility in organic solvents can be used in a hot-melt extrusion, a solvent coating, or a dry coating process. It's important to select the right excipient for any of these methods that we choose.

We need to understand physicochemical properties of the excipients and their effects on active pharmaceutical ingredient (API) release as mentioned to make sure that the taste masking doesn't impact drug performance.

What is the impact of the growing interest and attention paid by the regulatory authorities on product acceptability and patient compliance?

Boltri: From a more general perspective, the growing attention of the regulatory authorities is raising the bar for those companies that want to develop a product that is acceptable and is easy to be taken in order to be compliant with the current regulations.

The emphasis now is not only on the efficacy and safety of the product, but also the acceptability aspect. This would require additional tools and expertise that, from our perspective of CDMO, are not completely implemented in certain pharma.

This is now a regulatory requirement, so all the companies have to adopt and understand the concept of acceptability and patient centricity, not only as just a nice discussion points, but also as something that should be implemented as integral part of any future drug product development.

In addition to suitability of polymer excipient with respect to target release profile, what are the other considerations when using polymer coating, especially for pediatric products?

Mahmoudi: When you're talking about the polymer coating, basically it is a film coating system. So, we need to consider the whole system. The film coating system often contains excipients other than the taste masking polymer; for example, plasticizers, pore formers, anti-tacking agents, and glidants.

We need to pay attention to the safety and the toxicity of the whole formulation and to the use level of each component. The amount of polymer we use for coating for a target release profile depends on the size of the particles or the substrates, the surface area, and the shape of the particles.

For example, pellets and granules have a larger surface area when compared to mini-tabs and conventional tablets. If you're coating pellets or granules, which are more suitable for use in pediatric products, a higher amount of polymer is needed as compared as compared to the amount of polymer that is needed for coating mini tabs.

Likewise, the amount of other ingredients in the coating system, like glidants, that are needed to prevent sticking during the coating process might be different for pellet coating vs. mini tablets coating. The total amount of the coating excipients also should be within a range that is safe and acceptable for the final dosage forms, especially for pediatric ones.

Does the technology and formulation approach used for developing a more acceptable product have any impact on the overall product quality and safety?

Boltri: That's an important and comprehensive question, and represents basically the other side of the coin. When you start playing with some thickening agent or coating, it's mandatory to challenge and to make a risk assessment of the possible consequences on the bio-pharmaceutical properties of the final product.

A deep understanding of all the possible impacts on the absorption rates and area under the curve (AUC) and bioavailability – these are elements that need to be part of the formulation exercise, even when we try to improve the acceptability of the product. That should be a mandatory part of any development, even in just targeting an improvement in the acceptability of the product.

For an oral liquid product, how can we mask the salty taste without changing the pH?

Boltri: I understand the point – you want to change the pH and cannot change the molecule or its nature, and then you can apply a physical barrier, a coating. Special coating for taste masking and also minimizing some gastric irritations – this is a way you can address the challenges of a salt without modifying the pH.

How should we go about selecting flavor or taste masking systems for products that are bitter or drugs like cephalosporins or amoxicillin, which give off an odor?

Boltri: There is not a predefined rule, especially for odor. You can play with taste, but odors are more difficult to manage. Usually selecting the flavor and taste for products is driven by identifying the target population and within the frame of the target population you should select the flavor which is the best performing in terms of real taste management. I would say that coating is still the best option, but when you have a combination of taste and odor you have to also combine the approaches. You have to combine coating with flavor in order to synergize the different approaches.

Are ion exchange resins safe for taste masking?

Mahmoudi: Yes, they are safe for taste masking – ion exchange resins are high molecular weight polymers with cationic and anionic functional groups, but they are water insoluble, and they don't have absorption in the body. They have been used in several oral formulations for taste masking and are in the marketed products.

For pediatric products, we need to pay attention when we use any excipient for oral formulation. We have marketed safe products that contain ionic exchangers. But overall, yes, ion exchange resins are safe for taste masking.

Which methods are best for masking bitter botanicals in the nutraceutical industry, especially in industries where clean label excipients are preferred?

Boltri: This is an additional challenge because in the nutraceutical industry, the limitations in terms of the use of excipients, the quantity of excipient allowed, are stringent. So I understand that, in the nutraceutical industry, an exhaustive use of flavor is preferred compared to the use of functional excipients, such as for coating polymers and things like that. The limited choice for polymers is actually limiting the possibility to mask the taste for really bitter compounds.

What bitter blocking agents are in the FDA's inactive ingredient guide?

Boltri: I believe that there is no blocking agent approved so far in general, and especially in the inactive ingredient database.

Mahmoudi: Yeah. I think some sodium salts can be used, but again, we can get back to this question later to provide more information, but I think some salts can be used to mask bitterness of specific compounds maybe by interfering with the bitter taste receptors.

Is there any tool available for evaluation of taste flavor systems for optimization of tablets or liquids?

Boltri: There are multiple tools. I think the question is more how we can measure; how we can quantify; how we can drive optimization for taste perception and taste masking, especially in the pharma segment. There are multiple tools, and there is probably not one that is ideal. So you have customized dissolution testing, electronic tongue, some animal model, like the BATA

You can also develop your own analytical dissolution methods, using some biosimilar media, and also having a more appropriate hydrodynamic in order to mimic what's happening in the mouth. All these tools and methods are basically useful for a ranking different formulations, different technological approaches; it's quite difficult to consider these analytical tools as predictive of the quality of the taste masking and acceptability of the product.

What are the most successful products for taste masking in solid dosage forms on the market today?

Boltri: There are many, I have to say. There are examples of taste masking products recently approved using ion exchange resins.

KCL is another valuable example. We produce multiple tons, taste masked KCl using microencapsulation, suitable to apply a tiny coating to prevent the drug being released in the mouth and perceiving a salty taste. There are taste masked antihistaminic drugs on the market, especially for the children population, which is more sensitive to taste acceptance. Many antibiotics, especially for those that are administered as suspension, require a certain approach to taste masking and some coating for temporary suspension.

Anti-cough, such as quinoline derivatives, are highly bitter and benefit from a certain flavoring and coating approach for optimizing the taste and ensuring adherence. To not talk about paracetamol and ibuprofen – there are many of these products currently formulated in a taste-masked version.

How do you choose the taste masking agent, and how do you calculate the use percentage on the formula?

Mahmoudi: It depends on your dosage form and the target release profile. If you want to have ODT formulation and a certain release, then you are looking at a specific profile that will be different than for a liquid formulation.

Depending on the dosage form, we start planning and designing for a strategy that will get the target profile. It's a question that we need to be more specific about API and patient profiles to select the taste masking agent, and we need to go over all those factors that we discussed earlier.

Boltri: This would be a question of the level of the flavor, and the level of the sweetener. It's a matter of the population segments (i.e., pediatric, geriatric) and various cultural differences. That's another important point that needs to be considered during the formulation design.

Not all the population like the same level of the flavor, and there are idiosyncratic preferences, sometimes. We have experience with Japan, and we had first to learn which are their preferences in order to match the expectations for taste masking, but more generally, overall acceptability.

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