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CASE STUDY | ORAL DOSAGE

The excipient of choice for taste masking technology with Hot Melt Extrusion

SITUATION

Patient wellbeing and quality of life greatly depend on medicine acceptance. Excipients may taste bitter or irritate mouth and throat. Inherited defensive reaction of the body is to reject unpalatable taste. For this reason, various strategies to enhance patient compliance taking such oral medication have been developed, for example coating/encapsulation, complexing with camouflaging agents, taste neutralizing by intricate drug modifications, and so on. Though, for children, elderly and even some adults, swallowing solids (tablets/capsules/powders) possess a challenge. Thus, these consumers often take medicine in a liquid or suspension form. Sugars and sugar-free sweeteners reduce bitterness but show to be ineffective for strongly bitter agents.

Long chained compounds (polymers) could be used in this regard by “wrapping around” the drug, creating a barrier between bitter remedy and taste buds while keeping a drug in suspended state. On another hand, traditional solvent-based pharmaceutical production is complex and labor-consuming. Thus, a more robust, cost-effective, safe and easy to scale-up taste masking technology is in great need.

CHALLENGES

#1: Taste masking of bitter/irritable drugs is a must for pediatric oral medications,
#2: Need for easy to scale-up, environment-friendly manufacturing process of oral suspensions aiming towards high pediatric populations,
#3: Need for excipients in pediatrics that are as safe as possible.

SOLUTION

KLEPTOSE® Linecaps (KL) is a polymer (maltodextrin) obtained from pea starch and readily available in bulk. It has great potential for taste masking owing to origin, structure, and Hot Melt Extrusion (HME) processability. HME is a continuous solvent-free technique that originated from the plastic industry. A mixture of polymer matrix and other agents (such as, drugs) is melted, pushed, and blended together (extruded). The uniformed product can be milled/granulated/shaped in line with desired dosage form.

Material key benefits:

KLEPTOSE® Linecaps (KL) maltodextrin is ideal for pediatric oral suspension formulation because:

- KL is easily digestible and readily dispersible in water.
- KL materials comply with pharmaceutical and food regulations, particularly suitable for pediatric formulations.
- KL has low risk of allergic reaction (non-animal origin; made from non-GMO gluten-free pea),
- KL has potential to mask bitter taste by entrapping and bonding with a drug.

Processing key benefits:

Hot Melt Extrusion (HME) gained popularity in the pharmaceutical industry over traditional solvent-based methods due to:

- Absence of solvents, only heat and pressure are applied to melt a polymer-containing mixture,
- Continuous operation driving melted mixture through an outlet,
- Improved product quality and stability,
- Flexibility and cost-effectiveness.

RESULTS

1. HME parameters for KLEPTOSE® Linecaps (KL) maltodextrin established:

- Stability of all tested active and inactive ingredients at manufacturing temperatures has been confirmed (thermogravimetric studies, operating temps 150/155°C).
- A plasticizer (additive) has been required to make KLEPTOSE® Linecaps maltodextrin more rubbery and melt at lower temperatures, which is a common practice for HME of polymers. From a panel of 5 screened plasticizers, xylitol (sugar alcohol/food sweetener) was the most effective in decreasing the force (torque) required to drive the mixture through extruder.
- Acceptable xylitol content has a range (15 – 20% by weight), which provides a flexible window for formulation expansion. Other plasticizers are available on the market.
- Successful formulations of two model drugs have been prepared at: 70% KL/15% xylitol (plasticizer)/ 15% active ingredient (model drugs: griseofulvin (GRI) and caffeine anhydrous (CA) (named further HME granules)

2. Effective taste masking by KL polymer confirmed:

- Healthy human volunteers reported that oral suspensions prepared from HME granules of model drugs griseofulvin (GRI) and caffeine anhydrous (CA) tasted noticeably less bitter.

	GRI	CA
Physical Mixture	4.08	4.28
HME granules	1.5 ↓	1.83 ↓

Table 1 - Taste Score Given by Volunteers on scale 0-5 (5 most bitter)

- Dissolution studies in artificial saliva revealed a lesser drug release for both GRI (3 fold) and CA (2.5 fold) from HME granules, confirming stronger bounding of both drugs in HME granules and taste masking efficiency.

CONCLUSION

Taste masking is a challenging task which can be even more complicated when it comes to pediatric formulation. KLEPTOSE® Linecaps maltodextrin allows the delivery of an efficient taste masking solution with the total safety offered by a widely used food ingredient, manufactured to the critical quality standards of pharmaceutical excipient.

REFERENCES

1. Juluri A. , Popescu C., Zhou L., Murthy RN., Gowda VK., Chethan Kumar P., Pimparade MB., Repka MA., Murthy SN. ; *Taste masking of Griseofulvin and Caffeine anhydrous using Kleptose Linecaps DE17 by hot melt extrusion*; AAPS Pharm Sci Tech, 17 (1), 2016: 99-105