Orally disintegrating tablets (ODTs) are rising in popularity because of their ease of administration and improved patient compliance, creating the need for excipients that enable both taste masking and rapid disintegration. This article describes a method for taste masking ODT formulations by coating the active pharmaceutical ingredient (API) with an aqueous ethylcellulose polymer dispersion combined with different plasticizers.

A significant part of the global population—particularly geriatric, pediatric, and psychiatric patients—has difficulty swallowing solid oral dosage forms (SODFs). Approximately 40 to 60 percent of adults living in assisted-living facilities and nursing homes are reported to have trouble swallowing [1,2]. And each year, approximately 569,000 children, ages three to seven, also have difficulty swallowing [3]. Others who suffer from drug-induced dysphagia or deglutition disorders face similar difficulties. When developing a new drug product, it is imperative to formulate inclusive, patient-friendly options to enable compliance.
Orally disintegrating tablets

The ODT is a patient-friendly drug delivery solution that’s quickly rising in popularity because of its ease of administration, accurate dosing, and simple storage requirements. The global ODT market is predicted to expand at a compound annual growth rate of 11.5 percent, from $11.4 billion in 2017 to $27 billion by the end of 2025 [4].

Unlike other drug delivery systems and conventional immediate-release solid dosage forms, ODTs disintegrate in the mouth within 5 to 30 seconds without chewing or requiring water. ODTs are popular with hospitals and healthcare providers because they yield improved compliance, particularly for patients whose swallowing reflex is compromised, which is estimated to be up to 25 percent of hospitalized patients [5,6].

ODTs have also been widely supported in the pediatric realm, as the platform combines the administration flexibility of a solid dosage form with the swallowability of a liquid dosage form [7].

In addition to disintegration time, an ODT’s organoleptic properties (taste, aftertaste, and mouthfeel) are critical attributes because they impact patient acceptance and overall medication adherence. Since most APIs are bitter, sour, metallic, or otherwise unpleasant tasting, the API in an ODT must be completely taste masked while the tablet disintegrates, especially since the ODT remains in the mouth longer than other SODFs.

Taste masking ODTs

In recent decades, the pharmaceutical industry has invested heavily in new technologies and made great strides its ability to mask unpleasant tastes and odors. As a result, formulators have a broad range of format options and can now develop taste-masked drug products in the form of granules, films, tablets, and more.

One technology that is widely used for taste masking is the aqueous ethylcellulose dispersion (ECD). ECD polymers have been gaining popularity since 1958 but have most often been used for taste masking oral sustained-release dosage forms [8].

This article describes a study in which researchers demonstrated how to taste mask ODT formulations by coating the API with an ECD polymer prior to tableting. This method of taste masking works by physically trapping the porous powder in the thin, hydrophobic ECD matrix backbone, which masks the API’s bitter taste. The hydrophobicity of ECD can then be reduced by increasing its porosity via a suitable pore former, such as polyvinyl alcohol-polyethylene glycol graft copolymer. The coating can also help prevent gastric inactivation and hepatic metabolism of the API.

The researchers chose paracetamol as a model API because of its high bitterness and ease of availability and handling. For the ECD polymer, they chose DuPont’s Aquacoat ECD, which does not contain any plasticizer, so it provides formulation flexibility. By varying the solids content of the coating formulation and combining the ECD with different plasticizers, such as triethyl citrate (TEC) or dibutyl sebacate (DBS), formulators can optimize the tasting masking for the ODT dosage form. Because DBS provides improved film performance, quick coalescence, and improved taste perception, it is an ideal plasticizer for preparing an ECD-based dispersion for taste-masking purposes.

Coating the API

The researchers first prepared the coating dispersion by blending the ECD with the DBS plasticizer for a minimum of six hours to ensure homogeneity. A 10 percent w/w aqueous solution of polyvinyl alcohol-polyethylene glycol graft copolymer (Kollicoat IR) was added to the ECD dispersion to function as a pore former, and the dispersion was stirred for an additional 30 minutes.

For the coating trials, the researchers chose a paracetamol dose that was equivalent to a common clinical dose. As shown in Figure 1, they prepared the ECD and DBS coating dispersion (25 percent of EC solids) in a flu-
idized bed processor (ACG Pharma Technologies, GPCG 1.1) using a top-spray technique that applied the coating solution onto the paracetamol with optimized coating parameters. To ensure complete coalescence, the researchers cured the resultant granules for approximately 24 hours in a tray dryer with a thermal treatment at 60°C. The percentage composition of coating solution ingredients is listed in Table 1.

**Formulating the tablets**

The researchers then used direct compression techniques to formulate the ODT tablets, as shown in Figure 2. The formulation contained the taste-masked paracetamol granules, mannitol (Pearlitol 160 C), microcrystalline cellulose (Avicel PH-105) as compression aid, and 3 percent w/w croscarmellose sodium (Ac-Di-Sol SD-711) as superdisintegrant. All ingredients were passed through a #40 sieve and mixed in a blender for 10 minutes. The selected lubricant (Alubra PG 100), flavor, sweetener, and silicon dioxide (SiO2) were then sifted through a #60 sieve and added to the formulation.

The researchers mixed the coated paracetamol and the ODT materials into a uniform blend and compressed the blend into tablets using 12-millimeter round punches. The prepared tablets were evaluated for in-process quality parameters such as friability, hardness, disintegration, and dissolution. The percentage composition of tablet ingredients for the formulation is listed in Table 2.

**Conclusions**

While preparing taste-masked API granules, the researchers found that coating weight gain up to 25 percent w/w ECD-DBS dispersion yielded the most favorable results. The formulated tablets provided better sensory attributes compared to a commercially available formulation, as shown in Figure 3. As Figure 4 shows, the in vitro dissolution profile of the formulated tablet shows complete drug release in less than one hour, indicating no specific sustained barrier to drug release. The weight variation of
all the tablets was within acceptable limits of pharmaco-poeia standards. Overall, the coated particles saw improved flow characteristics and compaction properties.

When the model tablets were tested for in-process quality control and taste-masking performance, the researchers found that both the mouthfeel and disintegration time were acceptable to patients. Researchers noted that such characteristics could be improved by optimizing the coating parameters and ODT formulation design. By optimizing the parameters, manufacturers can ensure better product development, including efficient performance of ODTs with required taste-masking ability.

The model formulation shows that, by using ECD in fluidized-bed processor coating, drug product manufacturers can provide patient-friendly ODTs with a pleasant mouthfeel and good taste-masking qualities. This has the potential to both increase patient adherence and broaden the possibilities of APIs suitable for ODT formulation. T&C

References


Sreeramaiah Arunkumar is formulation & development scientist, technology & innovation, India; Michael Baumann is global strategic marketing manager, immediate release pharmaceutical dosage forms, Rina Chokshi is global leader for regional and field marketing, and Vinay Muley is leader, pharmaceutical excipients, technology & innovation, India, for DuPont Nutrition & Biosciences. For questions or comments about this article, please contact Lindsay Torriero, brand & global content leader, DuPont Nutrition & Biosciences (lindsay.torriero@dupont.com).