Co-processed excipients for Dispersible Tablets – Manufacturability and Patient Acceptability

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Introduction: Co-processed excipients are the combination of two or more excipients often prepared by spray drying, wet granulation and co-crystallisation. They may enhance functionality and reduce drawbacks compared to traditional excipients for the manufacture of tablets on a commercial scale; they may have a particular advantage in the development and manufacture of dispersible tablets. Typically, dispersible tablets should disperse quickly in minimal aqueous media with adequate palatability to enhance patient acceptability.

Aims: The aim of this study was to investigate a range of co-processed excipients in terms of manufacturability and patient acceptability using sensory analysis in human volunteers.

Methods: Sixteen co-processed excipients were screened based on manufacturability criteria and the best performing CPEs were selected for patient acceptability assessment. Excipients were blended for 2 min. at 22 rpm with 1% w/w sodium stearyl fumarate (lubricant), using a Turbula Blender. Placebo tablets of 500 mg, 10.5 mm diameter, round, convex, were prepared by DC using a Phoenix Compaction Simulator. Tablets were evaluated for compressibility, friability, disintegration time and fineness of dispersion. Nine excipients pre-selected based on manufacturability were evaluated in a randomised, preference and acceptability testing in 24 healthy adult volunteers. Patient acceptability was evaluated using 5-point hedonic scales (anchored from (1) “very acceptable” to (5) “very unacceptable”).

Results: The nine excipients pre-selected based on manufacturability criteria showed good compressibility, low ejection shear (≤ 2.63 MPa), low friability (≤ 0.25%) and rapid disintegration (≤ 47 s). Based on the sensory evaluation, the excipients were classified in order of acceptability as follows (from most acceptable): SmartEx QD100, F-Melt Type C, F-Melt Type M, MicroceLac, Ludiflash, CombiLac, Pharmaburst 500, Avicel HFE-102 and Avicel PH-102. All the co-processed excipients, except Avicel HFE-102, were significantly more acceptable than Avicel PH-102 ($p < 0.05$), which is non-co-processed excipient that was used as a control. An association was found between fineness of dispersion and acceptability, since the excipients that failed the 250-µm fineness of dispersion test were the least acceptable, i.e. Pharmaburst, Avicel HFE-102 and PH-102.

Conclusions: Overall, the most suitable co-processed excipients for dispersible tablet formulations were successfully identified. In particular, SmartEx QD100 and F-Melt Type C have been established within the top-3 excipients in terms of manufacturability, as well as in the top-3 excipients regarding palatability and acceptability, which makes them the most promising candidates for dispersible tablet formulations. However, the organoleptic profile of a dispersible formulation will be highly influenced by the organoleptic properties of the API and thus the formulation design (e.g. the need for taste-masking strategies) must be considered on a case-by-case basis.

Keywords: co-processed excipients, palatability, patient acceptability, dispersible tablet, organoleptic profile