# Palatability and Manufacturability Assessment of Dispersible Tablets Prepared Using Co-Processed Excipients with Different Active Pharmaceutical Ingredients

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**Introduction:** Dispersible tablets are used to treat a variety of patient populations. Primarily this is because both young and old patients report difficulty in swallowing conventional oral medications, resulting in poor compliance to the treatment. Preparation of dispersible tablet formulations using direct compression provides a simple manufacturing process. Ideally, a dispersible tablet formulation should exhibit good flowability and tabletability as well as offering a fast disintegration time and full dispersibility in a liquid media. Ensuring a dispersible tablet is palatable is also a crucial aspect of drug design. Co-processed excipients could be used as an alternative to conventional excipients to provide improved manufacturability and palatability of dispersible tablets prepared by direct compression.

**Aims:** The aim of this work was to assess 3 co-processed excipients, that have previously been shown to be promising in terms of manufacturability and palatability as standalone products, alongside 3 active pharmaceutical ingredients (API).

**Methods:** Co-processed excipients (F-melt type C, Pharmaburst 500 and SmartEx QD100) were lubricated and compressed into 10.5mm convex tablets with 3 model drug substances; API 1 (low bulk density), API 2 (fine particle distribution) and API 3 (high bulk density and coarse particle size distribution) at 5% w/w (and 20% for API 2) using a Phoenix Compaction Simulator. Compression profiles were produced using a range of compression forces and the generated tablets were assessed for hardness, friability, disintegration and fineness of dispersion. The ability of the co-processed excipients to improve palatability was assessed using the rat brief access taste aversion (BATA) model. The co-processed excipients and API 1 (with known aversiveness) at 5% were tested using the BATA model. Twelve male Crl: CD (SD) rats were exposed to each excipient, at 0.1mg/mL, and API, at 1mg/mL, with and without sweetener; sucralose at 0.1mg/mL. API 1 was used as it has previously been run through the BATA model and is aversive. Sucralose was used as a control as it is a commonly used sweetener.
All animal studies were ethically reviewed and carried out in accordance with the Animals (Scientific Procedures) Act 1986 and GSK Policy on the Care, Welfare and Treatment of Animals.

**Results:** F-melt Type C formulations using 5% of each API, performed consistently well, with excellent tabletability (Maximum tensile strengths > 3.0 MPa), excellent friability, short disintegration times (27-38 seconds) and good fineness of dispersion results. F-melt Type C was the only excipient that enabled tablet manufacture of API 2 at 20%. All other tablets produced to this specification demonstrated capping. These tablets had an unacceptably high disintegration time (approximately 27 minutes) and a high ejection shear (9.78 MPa), but they had acceptable friability and tensile strength. Formulations containing each API at 5% w/w with Pharmaburst 500 provided high maximum tensile strengths (> 2.75 MPa) and acceptable disintegration times (40-79 seconds). High ejection shear results were obtained with Pharmaburst 500 and API 2 at 5% w/w (> 5 MPa). SmartEx QD100 formulations with each API at 5% w/w again provided high maximum tensile strength (> 2.7 MPa) but had slightly longer disintegration times (43-118 seconds) and failed friability testing with API 3 due to tablet capping during the test. The BATA data showed no improvement in palatability for any of the co-processed excipients tested. The sweetener control also failed to improve the palatability of API1.

**Conclusions:** These results indicate the co-processed excipients tested can produce robust dispersible tablets which rapidly disintegrate with a range of API with different physical

properties. The lack of improved palatability by sucralose and the co-processed excipients, which all contain mannitol, suggest this API cannot be improved by sweetness alone and may require an alternative taste-masking approach. Future work could investigate if these co-processed excipients improve the palatability of a different API, perhaps one that is known to be improved by sucralose. The co-processed excipient could then negate the need for a sweetener and improve manufacturability.

**Keywords:** co-processed excipients, manufacturability, palatability, direct compression, dispersible tablets.