The Performance of a Tape Based DPI Device

Stephen Stein, Tom Robison, and Zhaolin Wang

3M Drug Delivery Systems, St. Paul, MN, USA

Background

The Taper DPI device uses a unique microstructure carrier tape (MCT) approach for defining the dose to be delivered to the patient (Figure 1). The drug is contained in small microstructure depressions ("dimples") in the MCT (Figure 2). Each dose is comprised of numerous dimples containing the drug. Prior to the delivery of each dose, a fixed amount of MCT (approximately 2.0 cm^2) is advanced into the dosing zone for delivery. Once the target flowrate has been achieved during dosing, a mechanical breath sensor releases an impact hammer which strikes the MCT and releases the drug powder from the MCT for delivery to the patient.

Figure 1: Taper DPI with Microstructured Carrier Tape (MCT)

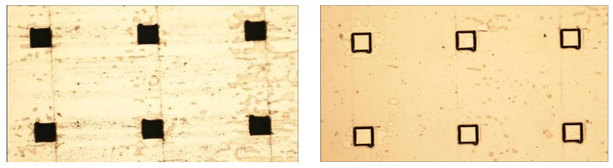

Figure 2. Images of Taper MCTs. Left image shows several dimples prior to being filled with drug; right image shows several dimples after being filled with drug.

The dose to be delivered is controlled by adjusting the size and number of the dimples contained in a given area of the MCT. Total powder doses of up to 1 mg of pure API are possible. The size of the dimples varies, but is typically between 50 and 200 microns in width and between 25 and 100 microns in depth. Various dimple geometries are possible, but often are truncated cones or pyramids (Stein et al, 2010). The number of dimples varies based on the dose, but is typically several hundred.

Operation of the Device

The Taper DPI has a simple-to-use and intuitive user interface that was developed based on the output of a large research study involving interviews with 100 asthma patients and specialty respiratory nurses (Fradley and Hodson, 2009). The development team met with patients (elderly, adult, and children) in their homes to gain insight into inhaler use in real-life settings. Patient interviews were conducted in the US, UK, and Italy. Numerous prototype Taper DPI concepts and other commercial DPIs were presented to the patients and nurses for feedback. Insights from these meetings were summarized and guided the development team, resulting in a device with the following features:

Features of the Taper DPI Patient Interface:

- Simple 3-step operation - MCT is advanced to prepare the dose when the patient opens the mouthpiece cover (Figure 3)
- 120 doses contained in pocket-sized device
- Visual feedback indicating when dose has been delivered
- Audible feedback to patient that dose has been delivered
- Dose-by-dose counter with large font size (font is 50% larger than *Advair® dose counter font)
- Low resistance, breath-triggered device

Figure 3, The Taper DPI patient interface

Excipient-Free Formulation Using Coated MCT

A high-throughput, asynchronous roller coating process is used to fill the dimples with the drug powder (Figure 4). The Taper MCT design and filling process allow for efficient and consistent drug delivery without the use of lactose excipient, thus eliminating the need to develop complex formulations. The total powder loading in the device is greatly reduced since there is no lactose, enabling the delivery of 120 doses in a pocket-sized DPI device.

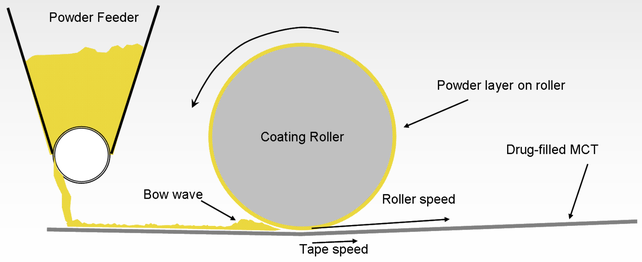

Figure 4. A schematic of the asynchronous roller coating method for filling drug into the dimples on the Taper MCT. The roller linear speed is often about 3 times greater than that of the MCT.

Dose Delivery from the Taper DPI

The drug delivery characteristics of Taper DPIs containing albuterol sulfate were characterized by measuring the aerodynamic particle size distribution and the emitted dose. Aerodynamic particle size distribution measurements were performed using the Next Generation Pharmaceutical Impactor ("NGI", MSP Corporation, Shoreview, MN) at a flowrate of 85 lpm, which resulted in a pressure drop of 4 kPa. Figure 5 shows the average of five size distribution measurements. The fine particle fraction (defined as the percent of the emitted dose smaller than 5 microns aerodynamic diameter) was 53%. The emitted dose was measured at 4 kPa using compendial apparatus and procedures (USP 2008). The emitted dose is shown in Figure 6 after various storage conditions with results showing all 70 of the measured doses being within +/-25% of the target dose and 69 of the 70 doses measured being within +/-10% of the target dose. Further details on the drug delivery from the Taper DPI, including through-unit drug delivery, can be found elsewhere (Stein et al., 2010).

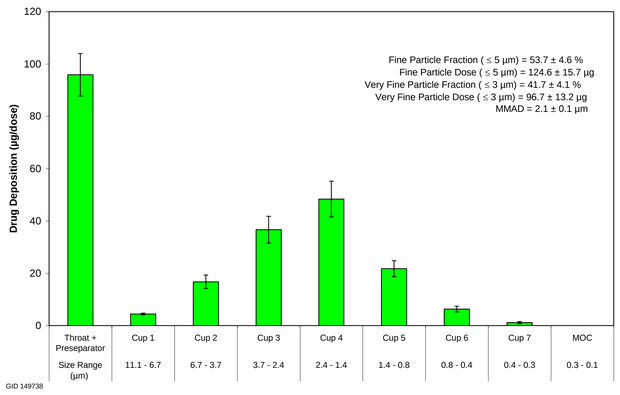

Figure 5. The aerodynamic particle size distribution of albuterol sulfate delivered from the Taper DPI (n= 5).

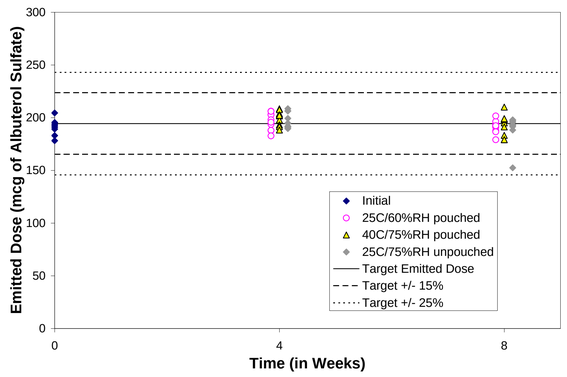

Figure 6. Emitted dose of albuterol sulfate delivered from the Taper DPI after storage at various conditions.

Taper Delivery After Exposure to Shock and Vibration

The geometry of the dimples has been optimized to retain the powder in the dimples prior to delivery, but enable the powder to be released when the hammer strikes the MCT during dosing. The van der Waals forces associated with the highly cohesive micronized powder formulations used in the Taper DPI help retain the powder in the dimples. In addition, the powder is further retained in the dimples by the fact that the MCT is tightly wound onto a spool prior to dosing.

The Taper device was subjected to high intensity vibration and drop testing to assess the retention and subsequent delivery of drug powder in the dimples on the MCT under possible stresses expected to occur during product distribution and patient handling. For the vibration testing, ten devices were tested following ASTM D4169, which specifies motion in all three axes at a frequency varied from 10-200 Hz. The specified vibration resulted in an accelerated spectral density of 1 m^2/s^2 (1.5G) for 30 minutes on each axis (90 minutes total). The albuterol sulfate emitted dose was measured before vibration and the next four doses were measured after device exposure to this high intensity vibration stress. The results show no statistical difference (p-value = 0.31) in emitted dose as a result of vibration stress when compared to the pre-vibration control tests (Figure 7a). The drug delivery of the Taper DPI after dropping was assessed by measuring the emitted dose prior to dropping, then after dropping onto a concrete floor from a height of 1 meter. The albuterol sulfate emitted dose was measured before dropping and the next three doses were measured after dropping the device. The results show no statistical difference (p-value = 0.44) in emitted dose as a result of dropping (Figure 7b). Figures 7a and b demonstrate the robustness of the drug delivery from drug coated Taper MCTs.

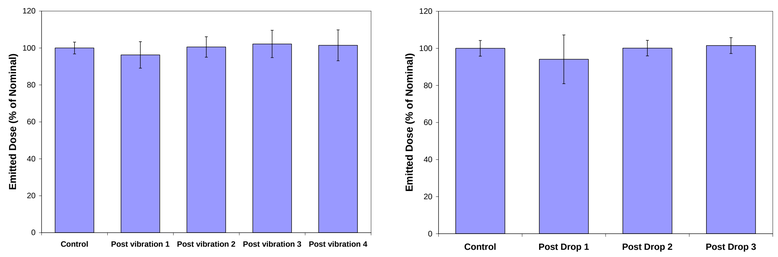

Figure 7a (left). Comparison of the emitted dose of albuterol sulfate delivered from the Taper DPI before and after vibration. Figure 7b (right). Comparison of the emitted dose of albuterol sulfate delivered from the Taper DPI before and after dropping.

Conclusions

The device utilizes a unique dimpled MCT to deliver pure API without the need for lactose excipient. A wide dosing range can be achieved by adjusting the size and number of dimples on the MCT. Drug delivery testing has shown that drug powder can be efficiently and consistently loaded into and released from the MCT. Drug delivery from the Taper DPI was shown to be insensitive to dropping and vibration mechanical stresses. By eliminating the need for lactose carrier, the challenges associated with generating ordered blends can be avoided and the size of the device can be reduced, enabling delivery of 120 discrete doses in a pocket-sized device.

References

Fradley, G., and Hodson, D. (2009), "Designing devices for multiple constituencies: designing a dry powder inhaler to meet regulatory requirements and cost restrictions while incorporating patient-friendly features", *Inhalation*, December 2009.

Stein, S., Hodson, D., Alband, T., Sitz, R., Robison, T., Wang, Z., Chiou, H., Simons, J., McNally, R., and Ganser, J. (2010), "The 3M™ Taper Dry Powder Inhaler Device," *Respiratory Drug Delivery 2010*, Orlando, FL, R.N. Dalby, P.R. Byron, J. Peart, J.D. Suman, S.J. Farr, P.M. Young (eds), Davis Healthcare Publishing International, River Grove, IL, USA, pp. 377-380.

US Pharmacopeial Convention (2008). "Aerosols, nasal sprays, metered-dose inhalers, and dry powder inhalers", United States Pharmacopeia 31 Chapter <601>.

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