Recent advances in drug delivery via inhalation have created a number of interesting opportunities for inhalation devices. New developments have helped make this delivery route compatible with larger molecules, such as proteins and peptides, and inhalation delivery can be used for both local and systemic drugs. With the new capabilities made possible by recent advances, inhalation may soon become the therapy of choice for a variety of conditions.

As the pharmaceutical community is aware, administering drugs via the lungs offers a number of benefits. Compared with drugs that must travel through the patient’s gastro-intestinal tract, inhalation can minimise systemic absorption and adverse effects. It also offers obvious benefits for treatment of respiratory diseases, including asthma and COPD. In addition, inhalation can play a role in delivering drugs for seasonal allergies and mass immunisations.

Within the field of inhalation technologies, dry-powder inhalers (DPIs) have seen a number of recent innovations, and they offer several advantages over aerosol-based inhalers. These devices can be used to deliver medicines that may not be compatible with an aerosol propellant formulation. Because the medicine in metered dose inhalers must be combined with propellants and other materials to work properly, this process may not be suitable for certain drugs. However, no propellant is necessary for drugs delivered via a DPI. Furthermore, DPIs have been shown to deliver more of the respirable-sized drugs deeper into the lung, enabling them to work more efficiently than other inhalation therapies. As they can be used with both lung-specific and systemic applications, DPIs give pharmaceutical developers valuable flexibility.

DPIs allow developers the ability to tailor the number of doses available, making them suitable for single-use applications such as vaccines. Furthermore, they are convenient for particular patient needs. For example, a parent may be wary of giving a child a metered-dose inhaler with a hundred doses of an expensive asthma drug. However, with DPIs, the drug can be dispensed more carefully.

3M Drug Delivery Systems has a long-standing reputation as an innovator in inhalation technologies, having introduced the first metered-dose inhaler and the first CFC-free propellant pressurised metered-dose inhaler. Today, more than half of all metered-dose inhalers worldwide utilise 3M technology.

Figure 1 shows a selection of 3M’s inhalation products, including 3M’s two recently introduced technologies in the DPI category – the 3M™ Taper Dry Powder Inhaler and the 3M Conix™ Dry Powder Inhaler. Continuing the company’s record of innovation, both products use unique design features to ensure efficient delivery of drugs and to simplify operations.

THE 3M TAPER DRY POWDER INHALER

The 3M Taper DPI (see Figure 2) has a proprietary design that stores active pharmaceutical ingredients (APIs) on a microstructured carrier tape (MCT). The inhaler uses 3M micro-replication and extrusion technology to create a “dimpled” tape upon which one or more APIs are coated, enabling it to provide up to 120 pre-metered doses. This dimple design allows the use of API only, virtually eliminating the need for lactose or complex powder formulations.

The device works via a simple mechanical process: upon opening the mouthpiece, a dose is ready for use. The air flow of the patient’s inhalation releases an impactor that strikes the tape and releases API into the airstream. API particles are further de-agglomerated as they pass through the device, helping to ensure effective delivery.
DESIGNED WITH “DIMPLES”

Key to this device’s method of action is the microstructured carrier tape. Prior to the delivery of a dose, a fixed length of the MCT is presented into the dosing zone within the device. The amount of API delivered with each dose is determined by the number of dimples on the tape, the volume of each dimple, and the density of API powder packed into the dimples; therefore, individual doses in the range from 100 μg to 1 mg are possible. The device can also be used to administer lower doses, but this may require blending the API with lactose.

The dimple geometry of the carrier tape is designed to provide a balance between API retention in the dimples throughout dimple filling and device storage, while promoting release of API from dimples during dosing. API is retained in the MCT dimples prior to delivery due to the high van der Waals forces and mechanical interlocking forces associated with cohesive micronised API. More than 90% of the API is released from the web during dosing.

MEETING NEEDS FOR PATIENTS AND PHARMACEUTICAL PARTNERS

To design the Taper device in a way that would meet the needs of patients and the medical community, 3M conducted patient use studies and interviewed healthcare providers in several global markets. Findings from this research revealed a number of important factors. From the patient standpoint, an easily transportable device that is small enough to be concealed in the hand was desired. An audible or visual indication that the dose has been taken was also found to be important, as was an intuitive design with a comfortably shaped mouthpiece. Additionally, a device with a non-medical appearance, at an affordable cost, was requested.

These insights were incorporated into the final design of the Taper DPI, which was engineered to be intuitive and easy to use for patients, while meeting the needs of healthcare providers, pharmaceutical companies, and regulatory agencies. The 3M Taper device incorporates these qualities into a single compact device which includes an intuitive three-step process to use (open - inhale - close), and has a ready-indicator feature in addition to a dose counter. Figure 3 shows the device in use.

The Taper’s simple-to-use features also help encourage patient compliance. The ready indicator changes from green to red and makes an audible click to let the patient know the dose has been delivered. The dose counter is designed with a large, easy to read font size to make the patient aware of when to obtain a new device. As requested by patients in the market research, the device size is small enough to be easily carried in a pocket and discreetly held in the hand. The device’s unique capability to deliver neat API, without the need to use large amounts of a lactose carrier, gives it the ability to hold up to 120 pre-metered doses in its small size.

The device has also been designed to withstand the rigors of real world use. Results of a vibration stress test show no statistical difference in the emitted dose between a pre-vibration device and a post-vibration one. In drop testing, all tested devices emerged intact and were fully mechanically functional after completion of dropping. Devices were confirmed to trigger upon exposure to inspiratory flow, proper web advancement was demonstrated, and the dose counters and ready indicators were fully functional, demonstrating the mechanical ruggedness of the device. Moisture protection has also been taken into consideration in the design of the product, to guard against moisture during both the device’s shelf life and during its use.
This approach is intended to make the metering of micronised API and coarse carrier particles, typically lactose, to add bulk to the formulation. Previous work has shown that impact events are more effective at de-agglomerating than airflow shear alone. As de-agglomeration occurs, the large lactose particles are flung to the sides of the cone and the lighter API particles are carried along by the air flow and exit the cyclone. Therefore, any API still adhered to lactose particles are re-entrained into the deagglomeration process rather than being emitted, typically to impact in the throat. Studies have demonstrated that the device is effective at holding on to large, non-respirable particles to improve the emitted respirable mass. Thus, Conix technology improves delivery to the lung as indicated by increased efficiency, and reduced throat and pre-separator deposition.

This technology brings high-efficiency API delivery to the passive DPI development arena using traditional “simple” formulations of API and lactose. The high efficiency of the device is promising for pharmaceutical companies that seek to deliver high-cost compounds while minimising waste, as well as those that utilise highly potent agents for which delivery to the lung needs to be maximised while systemic delivery is limited.

A PARTNER FOR GROWTH

The global market for DPI devices is large and rapidly growing, so 3M’s business model allows it to partner efficiently with pharmaceutical firms to develop drug treatments and solve formulation challenges. As data continues to mount on the unique benefits and capabilities made possible by inhalation therapy, 3M’s innovative solutions and its ongoing research and development help make it a valuable partner for pharmaceutical firms. The Taper and Conix technologies represent the latest examples of 3M’s robust capabilities in the inhalation field.

REFERENCES: