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Understanding Medicinal Drug Delivery Using Dry Powder Inhalers (DPIs)

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Dry powder inhalers (DPI) remain a vital part of our healthcare system due to their extensive use caused by a large number of respiratory patients globally. However, despite their wide use, their inherent inefficiency leads to drug wastage, poor therapy, and high costs to the end-user.

For a long time, dry powder inhalers (DPI) have been used for treating asthma, and other respiratory diseases, by delivering medication directly to the lungs. These devices have also been used for the delivery of antibiotics with dry powders also having the ability to be used for nasal inspiration for the treatment of local as well as systemic disorders.

Precise particle size control

When a person inhales orally through a DPI, the air starts moving at high speed within the device. The air lifts the powder sitting inside the DPI or helps to move a capsule that contains the powder. This high-speed airflow eventually helps to aerosolise the drug within the DPI chamber. The chamber, designed to intensify the turbulence of the inhaled air, facilitates the collision of particle clusters with the chamber walls, helping them to “de-agglomerate” into fine particles of the size of a few microns (this is what we want to get to the lungs). Following this complex process, the fine aerosol exits the device and travels to the lungs through the patient’s mouth and airway.

However, along the way, many of the drug particles can stick to the device wall, the mouth, or the upper airway. So herein lies the inherent problem with DPIs. When a person inhales through the DPI, they do not actually know how much medicine

will be delivered to their lungs. The ‘dose’ stated on the device is not necessarily what will reach the lung, so much of it will be lost to the mouth and the upper airway. In some cases, up to 70 per cent or more of the powder lands on the airway, before it reaches the lungs.

The final mass of the desired dose, related to what we know as the ‘fine particle fraction’ (FPF) from the DPI, is governed by many factors, including drug morphology, inhalation pattern, and device design. Generally, only particles of the size ranging from 1 to 5 microns are counted as part of the FPF and they are the ones expected to reach the lungs. Too large a particle will end up in either the mouth, throat, or upper part of the airway. And if it's too small, less than approximately 1 micron, the chances of it getting out during exhalation are very high. Thus, precise particle size control is needed for efficient medicinal delivery when using a DPI.

For an everyday user, the drug's composition and the device's ease of use are the key driving factors when choosing a DPI. The quality of the medicinal aerosol and how much medicine will be delivered to the lungs isn’t really something a user thinks about too much, despite how important it is. The form of the actual particles in the inhaler is one key aspect which dictates control over the amount of finally delivered aerosol. In general, two ways of aerosolisation are preferred by commercial DPI manufacturers: a pure active ingredient and drug particles mixed with larger ‘carrier particles’. In both of these cases, small particles can undesirably join together into large agglomerates, which need to be broken up into small particles so that they can reach the lungs.

Unfortunately, it is almost certain that a proportion of ‘agglomerates’ will not disperse into a fine aerosol, and these will end up either staying in the device, or landing in the mouth, throat, or upper airways instead of lungs, thus leading to medicinal wastage and poor therapy. A simple solution to this problem would be to decrease the level of ‘stickiness’ between particles by decreasing the contact surface area available. Less contact surface area means less stickiness between particles. Creative solutions to this problem involve changing features such as the shape of the particles or adding corrugations.

Changing the shape helps in two ways: one, owing to the more streamlined aerodynamic shape, particles can start flowing within the inhaled air more effectively, thus increasing their chances of reaching the lungs. Second, the agglomerates formed are expected to have a higher porosity which minimises the need for too much of an additional aerodynamic force to break them up into smaller particles. Equally as important as improving the characteristics of the drug formulations is enhancing the design of DPIs, both in terms of ease of use, but also aerodynamic performance.

We can think of the design requirement from a modern DPI from two perspectives: how well does the drug evacuate from the device? Second, how effectively can it promote drug aerosol formation towards the goal of maximising FPF? Commercial devices use several design features to achieve these; for example, the outlet of the Turbuhaler has projections that induce a swirling turbulent motion of the air; the Easyhaler has a constricting air path at the inlet of the powder pocket to generate localised turbulence; and the NEXThaler design produces a swirling air motion above the powder bed. Most of these DPIs have unique features to attain high drug evacuation and dispersion. Though the integration of design features enhances the fluid-flow dynamics of the DPI, the gain in the finally-delivered drug is not always clearly linked just to device-level design attributes.

Factoring breathing profile

A recent study by the authors published in the International Journal of Pharmaceutics informed that the quality of the finally-delivered drug improves significantly if the flow is neither very smooth nor very chaotic/turbulent. Too ‘smooth’ and the particles don’t get out of the inhaler, and too ‘chaotic’ and too many of them land on the walls of the inhaler, so perhaps there is a ‘goldilocks’ zone for effective DPI usage. Additionally, the device design requires accounting for the complexities of human physiology. A key aspect of this physiology is the unique breathing profile of every person, which can change depending on the age and disease state.

Similar to our fingerprints, breathing patterns vary from human to human. The age, severity and type of disease, and physical build add to the variability in breathing. For example, a younger person would have fast breathing compared to an older adult. The variation in the breathing patterns leads to significant variation in the finally-delivered dose from person to person. Since it would be impractical and costly to design an inhaler for each person, suiting their breathing requirements, it is necessary to focus research towards investigating the impact of transient breathing and adapting DPI design accordingly.

Recently, we at the University of Sydney (Australia), and IIT Mandi (India), have started looking at the impact of various breathing patterns on detailed DPI particle flow behaviour. The initial results are promising, and we feel that integrating the effect of transient breathing as a normal part of the design of any inhaler would be a substantial improvement.

Improvements warranted

In conclusion, DPIs remain a vital part of our healthcare system due to their extensive use caused by the large number of asthma/respiratory patients globally. However, despite their wide use, their inherent inefficiency leads to drug wastage, poor therapy, and high costs to the end-user. Therefore, significant improvement in DPI design and drug morphology is warranted. Expectantly, synergistic integration of design and flow features, drug morphology, and adaptation of transient breathing would definitely enhance the efficacy of DPIs.

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