Advancing DPI Technology

A modular approach on optimizing capsule movement for improved performance

Mirjam Kobler[1], Daniel García Sabido[2], Martí Giralt Carbó[2], David Valencia Pellisa[2], Ameet Sule[3], Sunita Sule[3].

[1] H&T Presspart, Marsberg, 34431, Germany

[2] H&T Presspart New Product Development Centre (NPDC), L'Arboç, 43720, Spain

[3] H&T Presspart Inhalation Product Technology Centre (IPTC), Blackburn, BB1 5RF, United Kingdom

KEY WORDS: Dry Powder Inhaler (DPI), Rapid Prototyping, 3D Printed Modular Prototype, High Speed Camera, Enhanced Capsule Motion, Impact Frequency.

INTRODUCTION

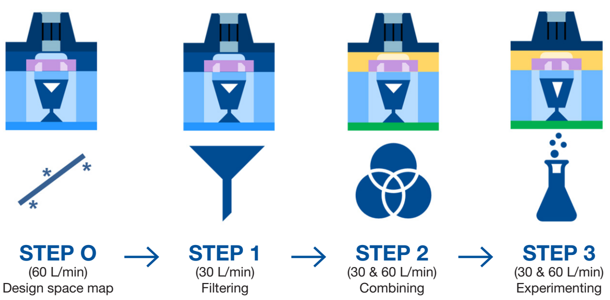
The field of pulmonary delivery within the area of dry powder inhalers is moving more and more towards engineered formulations, introducing new challenges of powder de-agglomeration in the device. This paper focuses on pioneering the oscillating motion of the capsule within the Sunriser© Dry Powder Inhaler (DPI) [1] device. Capsule movement is crucial for ensuring effective powder evacuation and overall performance [2], representing a critical aspect of device design.

In order to efficiently screen various device dimensions for optimal capsule movement, a modular prototype approach was adopted. This study emphasizes the advantageous role of rapid modular prototyping in developing a robust design capable of accommodating the inherent variability in capsule motion. This ensures continuous movement and, consequently, effective evacuation.

MATERIALS AND METHODS

The methodology used to achieve the optimized dimensions for enhancing the capsule motion was divided in 4 steps, namely STEP 0, STEP 1, STEP 2 and STEP 3 (Figure 1).

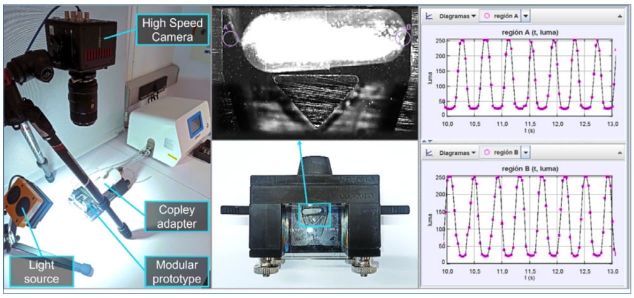
Figure 1 – Methodology strategy based on steps.



First, a design space map was systematically generated through stepwise modeling during STEP0, where one dimension at a time was varied at 60 L/min of the initial Sunriser© prototype while keeping other dimensions constant. Fifteen studies were conducted, identifying key dimensions that potentially influence capsule movement and determining its statical significance in the generated models. STEP0 laid the foundation for subsequent steps. STEP1 scrutinized modular prototype combinations evaluated at 60 L/min in STEP0, assessing their performance at 30 L/min. STEP2 further broadened the assessment, exploring new modular prototype combinations with modifications to multiple dimensions. Finally, continuing this exploration, STEP3 evaluated new modular prototype part combinations and designs at both 30 and 60 L/min, building on prior results. Throughout all steps, the evaluation had consistency by employing the same response variable (impact frequency) as STEP0, with the nominal modular prototype serving as the reference and control value.

The modular prototype combinations, connected to a flow controller (TPK 100i-R and DFM200 from Copley), underwent evaluation at specific flow rates (namely 30 and 60 L/min). A high-speed camera, in conjunction with a light source, captured capsule movement, and the resulting videos were processed using an acquisition software and analyzed with Tracker software (version 6.1.3 from Open Source Physics) (Figure 2).

Figure 2 – Testing set-up, modular prototype images, and example of analysis using Tracker.



The Tracker software has the capability of detecting changes in grey scale within the video, allowed for the precise identification of capsule impaction against the lateral walls of the DPI capsule chamber. From this value, an impact frequency is calculated. This metric considers how many times the capsule hits any of the two walls per second. All experiments were conducted using 3D-printed modular prototypes to assess capsule motion and evacuation in the DPI device.

H&T PRESSPART

Impacting Tomorrow. Together.

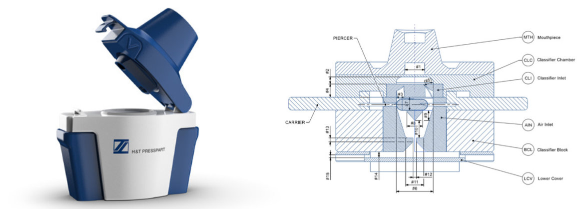
Advancing DPI Technology

A modular approach on optimizing capsule movement for improved performance

RESULTS AND DISCUSSION

The modular prototypes comprise of several interchangeable parts, allowing for a swift evaluation of the main dimensions influencing the design (Figure 3).

Figure 3 – Modular prototype design and dimensions identification.



The generated design space map reveals influential dimensions affecting capsule motion (impact frequency) within the DPI (Table 1).

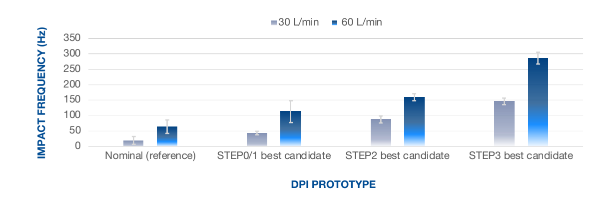
Table 1 – Results for the design space (STEP0) at 60 L/min.

Dimension	Range evaluated	Model p-value ≤0,05	Dimension direction for impact frequency increase
#1 – MTH Diameter	9.0 – 11.0 mm	×	-
#2 – CLC Height	2.6 – 4.6 mm	×	-
#3 – CLI Width	3.6 – 4.4 mm	×	-
#4 – CLI Height	6.5 – 6.9 mm	×	-
#5 – CLI Angle	20 – 50 °	✓	↓
#6 – AIN Chamber Width	17,3 – 19,9 mm	✓	●
#7 – AIN Chamber Height	6.5 – 7.2 mm	✓	↑
#8 – AIN Splitter Width	6.0 – 10 mm	✓	↓
#9 – AIN Splitter Height	3.0 – 7.0 mm	×	-
#10 – AIN Inlet Height	7.4 – 10.3 mm	✓	↓
#11 – AIN Inlet Width	7.0 – 11.0 mm	✓	↑
#12 – AIN Restrictor Width	1.5 – 2.1 mm	✓	↑
#13 – AIN Restrictor Height	1.8 – 2.2 mm	×	-
#14 – LCV Access Volume	0.9 – 2.5 mm³	✓	↑
#15 – LCV Access Area	24 – 57 mm²	✓	↑

It was observed that several dimensions, particularly those closely tied to fluid dynamics near the capsule, played crucial roles in influencing capsule motion. It is worth noting that dimensions seemingly unrelated to capsule motion (#1 to #4) may potentially impact Aerosolized Particle Size Distribution (APSD) downstream.

Table 2 shows the results at 30 and 60 L/min detailing the impact frequency obtained with the best candidates in terms of capsule motion identified in each step.

Table 2 – Impact frequency results evolution for each step.



Through the stepwise refinement, the DPI's capability to induce capsule movement has seen a remarkable enhancement. The optimal outcomes achieved at both 30 and 60 L/min, when contrasted with the reference nominal configuration, showcase a significant improvement. This improvement, compared with the best candidate identified in STEP3, reflects a performance increase of over seven times for capsule motion efficiency against the reference nominal design at 30 L/min.

CONCLUSIONS

The achieved substantial enhancement guarantees a robust and consistent capsule motion within the flow rate range from 30 to 60 LPM. The proposed methodology has played a pivotal role in exploring the performance of the novel DPI design. This approach facilitated informed design iterations, leading to notable advancements in capsule motion. Our systematic approach not only clarifies DPI performance but lays the groundwork for future advancements. Rapid prototyping and testing accelerate development of improved DPI designs, marking a leap towards more effective respiratory drug delivery.

References

[1] Groß R, Berkenfeld K, Schulte C, Ebert A, Sule S, Sule A, Lamprecht A. State of the Art in Capsule-Based Dry Powder Inhalers: Deagglomeration Techniques and the Consequences for Formulation Aerosolization. Pharmaceutics 2022, 14, 4.

[2] Shur J, Lee S, Adams W, Lionberger R, Tibbatts J, Price R. Effect of Device Design on the In Vitro Performance and Comparability for Capsule-Based Dry Powder Inhalers. AAPS Journal 2012, 14, 1185.

Acknowledgements

This study was funded jointly by Hovione and H&T Presspart.