ENHANCING PERSONALISED MEDICINE: POWDOSE AND DIFFUCAPS FOR PRECISE ORAL SOLID DOSING

Thierry Jomini, **Stéphane Baronnet** and **Dr John van den Anker**, all of **AbbatiaLabs**, along with **Giuseppe De Franza** of **Adare Pharma Solutions**, evaluate the performance of the POWDOSE® system in delivering precise and repeatable doses of different formulations of Diffucaps®. The authors analyse the functionalities of combining Diffucaps with POWDOSE and highlighting its potential for improving personalised dosing regimens.

Accurate dosing of oral solid forms is increasingly recognised as crucial for achieving optimal therapeutic outcomes while minimising adverse effects.[1] Indeed, the era of the "one-tablet-fits-all" is in the past. Patients now seek personalised treatments for their individual needs. Tailoring drug doses will facilitate precise titration (e.g. in neurological diseases, ADHD[2] and cardiovascular diseases[3]), help mitigate the development of antibiotic resistance[4] and enable weight-based dosing, particularly in paediatric populations.[5] Such individualised approaches are therefore critical for enhancing the safety, efficacy and overall effectiveness of treatment regimens.

Figure 1: POWDOSE device.

AbbatiaLabs has developed a novel dosing technology that enables precise dose titration for oral solid medications by the end user. The POWDOSE device, a two-step mechanism, allows users to first preset the desired dose using a ring and then accurately dispense the medication by turning a knob. This user-centric design is optimised for ease of use and aims to minimise the risk of dosing errors, enhancing the reliability and safety of self-administered treatments (Figure 1).

Adare Pharma Solutions' Diffucaps technology is a multiparticulate system that uses polymer membranes to create multilayered beads, allowing precise drug release and enhanced solubility in targeted gastrointestinal regions. Diffucaps can minimise side effects, such as gastric irritation, and reduce the impact of food on absorption.

This article evaluates and assesses the performance of the POWDOSE system in delivering precise and repeatable doses of different formulations of Diffucaps, demonstrating the system's capacity to achieve consistent and reproducible dosing.

TEST MATERIAL

The POWDOSE device can deliver incremental doses constituting a fraction of the maximum deliverable amount. The technology is fully customisable, allowing adjustment of both the number of increments and the maximum dose to suit the specific requirements of the administered medication. In this study, four (1–4) POWDOSE devices were manufactured and tested. Each device was evaluated for its ability to deliver four distinct dose sizes, corresponding to 25%, 50%, 75% and 100% of the maximum deliverable dose. The reservoir was customised to accommodate up to 30 full-dose deliveries (Table 1).

Dose Percentage (max)	Doses
25%	120
50%	90
75%	60
100%	30

Table 1: Percentage of max delivered dose for this device configuration with the corresponding number of doses delivered.

"THE POWDOSE DEVICE, A TWO-STEP MECHANISM, ALLOWS USERS TO FIRST PRESET THE DESIRED DOSE USING A RING AND THEN ACCURATELY DISPENSE THE MEDICATION BY TURNING A KNOB."

With the flexibility needed to meet diverse patient requirements, Adare's Diffucaps can be used in multiple dosage forms, including capsules, orally disintegrating tablets, rapidly disintegrating tablets and sprinkle formulations. When combined with other Adare technologies, Diffucaps can enhance solubility, broadening its applicability across various drug compounds and therapeutic areas.

For the purpose of this study, Diffucaps sugar sphere core granules were used for testing. These granules did not contain any API, meaning that no specific therapeutic dose was targeted or considered during the testing. As a result, the mean delivered dose for each dosing series was not compared with a predefined or target delivered dose. Instead, the study focused on evaluating the device's ability to consistently deliver precise and reproducible increments of the granules across the specified dose fractions. This approach allowed for a comprehensive assessment of the device's performance in terms of dose precision, independent of any therapeutic dose considerations:

- Devices #1, #2 and #3 were tested with Diffucaps sugar spheres size 30 LOT: 2310458 (sphere diameter between 500 and 700 µm).
- Device #4 was tested with Diffucaps sugar spheres size 18/20 LOT: 2410135 (sphere diameter between 800 and 1,000 µm).

TEST SETUP

The devices were fully loaded with the sugar spheres for the test. Each device was mounted on a laboratory stand positioned above a calibrated KERN F1 balance (capacity 240 g, precision 0.001 g). The test engineer operated the device per the test protocol, delivering the doses into a receptacle placed on the balance, which was used to measure the amount of material dispensed by the device during each test iteration.

The testing sequence for each device was as follows:

1. 30 deliveries at the maximum dose
2. 60 doses at 75% of the maximum dose
3. 90 doses at 50% of the maximum dose
4. 120 doses at 25% of the maximum dose.

Each delivery was logged in a test sheet.

METHODOLOGY

The objective of this study was to evaluate dose delivery variability by a device during its development, rather than to establish a quality control release testing protocol. A straightforward approach was employed, focusing on the total variability of the assay and the variability observed at different dosing stages (beginning, middle and end of the dosing process). As already described, placebo Diffucaps granules were used to assess the variability in the mass of doses dispensed by the device. Statistically, the relative standard deviation (RSD) is considered a practical acceptance criterion.

While the European Pharmacopoeia 2.9.40 on Uniformity of Dosage Units was referenced, the T value was not applied due to the absence of API in the granule batch tested. Instead, the limit of ±25% of the mean value was considered the critical parameter. Therefore, for the test to be considered successful, dose could not deviate by more than ±25% from the mean value.

The test was passed if the RSD was <7%, or if all doses were within ±25% of the mean for each device.

% of Maximum Dose	Type of Diffucaps Granules	Devices Tested	All Values Are Within ± 25%	RSD	Target Value	Min and Max Values
25	Sugar spheres 500–700 µm	#1, #2, #3	Yes	< 1.5%	142 mg	133 mg < x < 154 mg
50	Sugar spheres 500–700 µm	#1, #2, #3	Yes	< 1.4%	285 mg	255 mg < x < 297
75	Sugar spheres 500–700 µm	#1, #2, #3	Yes	< 1.2%	428 mg	413 mg < x < 461 mg
100	Sugar spheres 500–700 µm	#1, #2, #3	Yes	#1 < 0.75% #2 6.7% #3 < 0.75%	570 mg	558 mg < x < 585 mg #2 2 doses at 412 mg & 428 mg

Table 2: Results for X% of the maximum delivered dose with devices #1, #2 and #3.

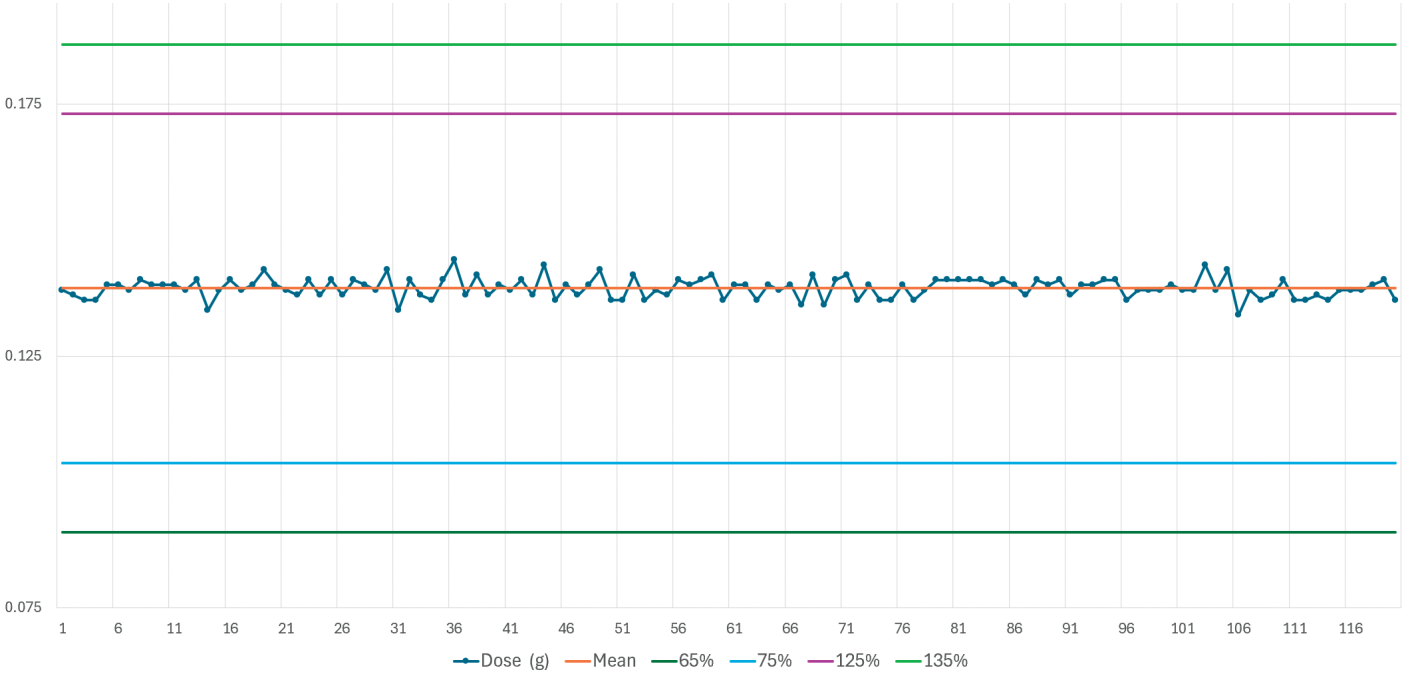

Figure 2: Delivered doses for targeted 25% of max dose with sugar spheres between 500 and 700 µm.

RESULTS

The results are summarised in Table 2. Figure 2 shows the delivered doses (g) targeted for 25% of the maximum dose with sugar spheres between 500 and 700 µm. Following the test with the sugar spheres 500 < x < 700 µm, another lot of Diffucaps sugar spheres was tested with a higher particle size: Diffucaps sugar spheres 800 < x < 1,000 µm. The results are shown in Table 3. Figure 3 shows the delivered doses targeted for 25% of the maximum dose with sugar spheres between 800 and 1,000 µm.

DISCUSSION

With 1,200 doses administered, the POWDOSE device demonstrated high precision and repeatability in delivering doses of Diffucaps sugar spheres. It is important to note that the devices used in this study were pre-production prototypes that have not yet undergone full industrialisation. As a result, the inner surfaces of the devices have not been optimised to minimise friction between the granules and the device walls. This optimisation will be addressed during the development and industrialisation process, which will occur prior to the product's commercial release.

In typical usage, the POWDOSE device will be manipulated by the user between dose deliveries. This handling introduces slight shaking, which helps to prevent issues such as granule bridging, clogging, or sticking – phenomena that likely contributed to the two low doses observed in the fixed-device test setup.

The results also indicated that the doses remain consistent throughout the entire usage period of the device: 30–120 doses. No variation in dose delivery was observed, regardless of whether the

% of Maximum Dose	Type of Diffucaps Granules	Devices Tested	All Values Are Within ± 25%	RSD	Target Value	Min and Max Values
25	Sugar spheres 800–1,000 µm	#4	Yes	< 1.9%	130 mg	118 mg < x < 133 mg
50	Sugar spheres 800–1,000 µm	#4	Yes	< 1.5%	261 mg	248 mg < x < 270
75	Sugar spheres 800–1,000 µm	#4	Yes	< 3.0%	394 mg	347 mg < x < 443 mg
100	Sugar spheres 800–1,000 µm	#4	Yes	< 3.1%	525 mg	480 mg < x < 574 mg

Table 3: Results for X% of the maximum delivered dose with device #4.

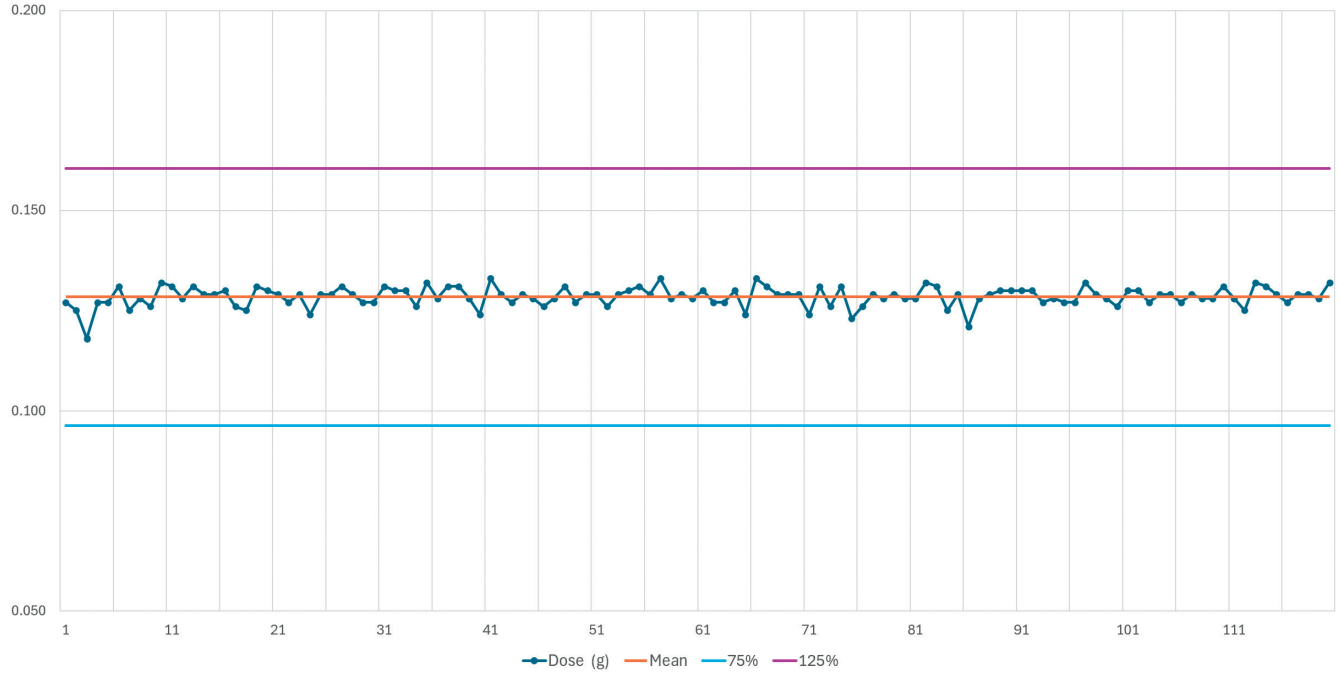

Figure 3: Delivered doses for targeted 25% of max dose with sugar spheres between 800 and 1,000 µm.

dose was administered at the start of the device's use (with a full reservoir) or at the end of its lifetime (when the reservoir was nearly empty).

Overall, the results indicate that Diffucaps granules in combination with the POWDOSE device provide a reliable and adequate solution for delivering customised doses of oral solid dosage forms. It provides a valuable tool for drug, chemistry, manufacturing and controls formulation teams, offering a means for patients to self-administer personalised doses of solid drugs with high accuracy and ease.

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