Powdose – Innovative dosing device for paediatric patients

Sikai Wang[1] ; Smita Salunke[1] ; Thierry Jomini [2]

[1]University College London School of Pharmacy, London,UK [2] AbbatiaLabs, Chemin de Pramey 18 1530 Payerne

INTRODUCTION

Current dosage forms for the pediatric population often lack dose flexibility, increasing the risk of medication errors . Addressing this issue, innovative formulations like granules, minitablets are being developed; however, their effective administration requires suitable delivery devices. The emerging 'Powdose' delivery device (Figure 1) is being developed to provide effortless dose adjustments and user-friendly operation for dosage forms such as powders, granules. However, understanding how these dosage form characteristics impact dosing accuracy and formulation administration through this novel device is crucial. This project aims to characterize various dosage forms, such as powders and multiparticulates, assessing the effect of flowability on administration via the Powdose device.

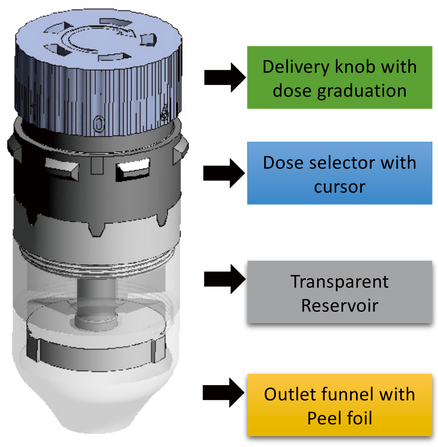


Figure 1

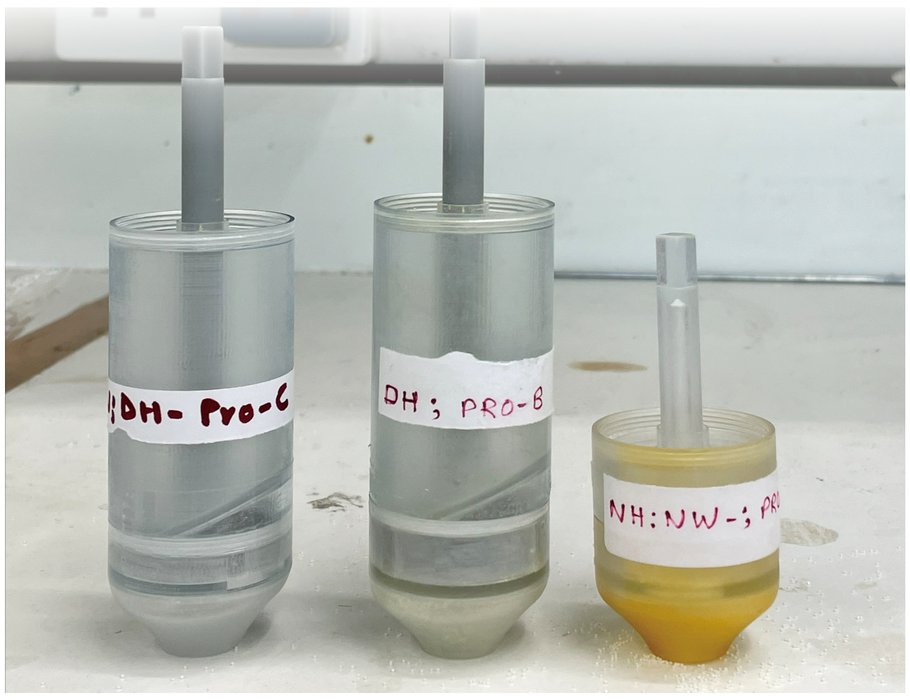
AIM AND OBJECTIVES

This project aims characterize various dosage forms, such as powders and multiparticulates, assessing the effect of flowability on administration via the Powdose device.In addition, the administration characteristics such as angle of administration were assessed to identify critical material and process attributes of the product that affect the product performance.

METHOD

1 Determination of flowability for selection of samples for device performance study
Several powder samples and multiparticulates were evaluated for flowability using a Pharmacopeial method (Ph. Eur. 11.0). In the European Pharmacopoeia, the evaluation of drug flowability requires the use of the Hausner ratio (HR). The Hausner ratio (HR) is calculated by dividing the bulk density (ρ bulk) by the tapped density (ρ tapped).

2 Determination dose delivered with different prototypes at different knob settings
Samples demonstrating favourable flowability were chosen for dose delivery testing using three distinct prototypes (A, B, and C). Six combinations of samples and device designs (2 samples x 3 device designs) were assessed, ensuring doses were administered at a consistent 90° angle to select the best design or recommend changes required. Recorded measurements included the actual dose delivered at three knob settings, reflecting the dose volume. The prototype consistently demonstrating accurate dose delivery with both powders was selected for further accuracy testing with other chosen samples.



3 Determination of dose delivered at different angle of administration
To ensure the accuracy of the angle of measurement, a simple model with a wooden board and bracket was created. A simple model with a wooden board and a stand. The wooden board has a standard isosceles right triangle. For 90-degree measurements, the drug delivery device was aligned parallel to the right-angled side and held securely in place with a bracket for accuracy studies. For 45-degree measurements, align the drug delivery device parallel to the hypotenuse and securely fasten it with the bracket for accuracy studies.

RESULT

1 Flowability results (Table 1)

Sr. No	Material	Type	Tapped density	Bulk density	Carr index	Hausner ratio	Flowability
1	Tri-calcium phosphate	Powder	0.69	0.56	19.48	1.24	fair
2	Kollidon®	Powder	0.57	0.45	21.05	1.27	passable
3	Lactose PrismaLac® 40	Powder	0.69	0.63	8.56	1.09	excellent
4	CO-AMOXI Mepha	Powder	0.74	0.48	35.14	1.54	very poor
5	DAFALGAN® Direct	Granules	0.74	0.64	13.51	1.16	good
6	Poloxamer 188 EMPROVE ® EXPERT	Granules	0.63	0.63	0.00	1.00	excellent
7	Creon® Micro	Granules	0.74	0.74	0.00	1.00	excellent
8	Neotylol Grippe	Granules	1.00	0.87	13.00	1.15	good
9	Magnesium-DIASPORAL®	Powder	1.00	0.83	17.00	1.20	fair
10	Veractiv Magnesium	Granules	1.00	0.77	23.00	1.30	passable
11	Cellets 350	Cellets	0.91	0.80	12.09	1.14	good
12	Cellets 500	Cellets	0.91	0.86	5.49	1.06	excellent
13	PKS C350	Cellets	0.91	0.85	6.59	1.07	excellent
14	PKS C500	Cellets	0.89	0.85	4.49	1.05	excellent
15	PKS C700	Cellets	0.91	0.87	4.40	1.05	excellent

Table 1

Placebo Kolicaoat SmartSeal coated bead C350 and Cellets 500 showed excellent flowability and narrow particle size distribution(PSD).

2 Dose delivered with different protypes with different knob settings(Figure 3, 4 and 5).

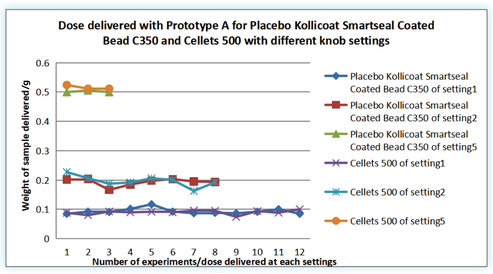


Figure 3

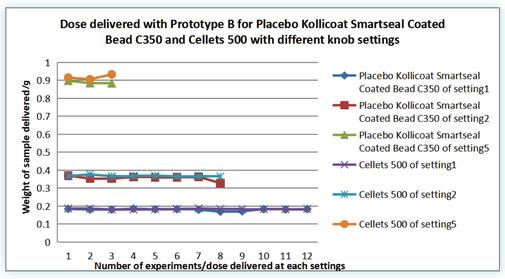


Figure 4

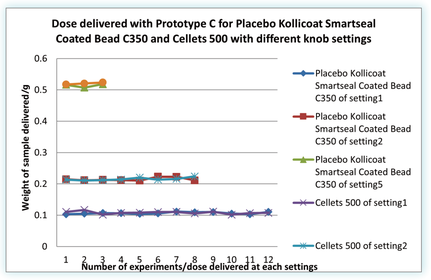


Figure 5

All equipment prototypes show good accuracy performance. However, equipment prototype A and C was eliminated because of its narrow storage volume, which could not meet the requirements of the initial storage volume test. Therefore, the device prototype B is finally selected as the main test device.

3 Dose delivered with selected prototype for different samples with good flowability (Figure 6).

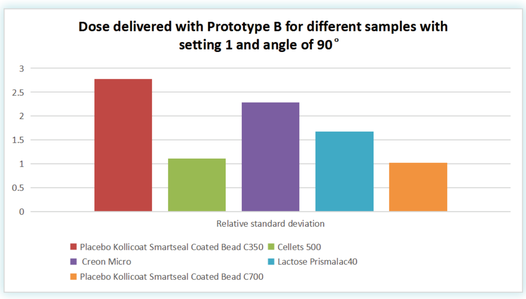


Figure 6

As for their relative standard deviations, their relative standard deviations are all between 1-2, which proves that the device is qualified for the drug administration accuracy of each sample under this condition.

4 Dose delivered at different angle of administration (Figure7).

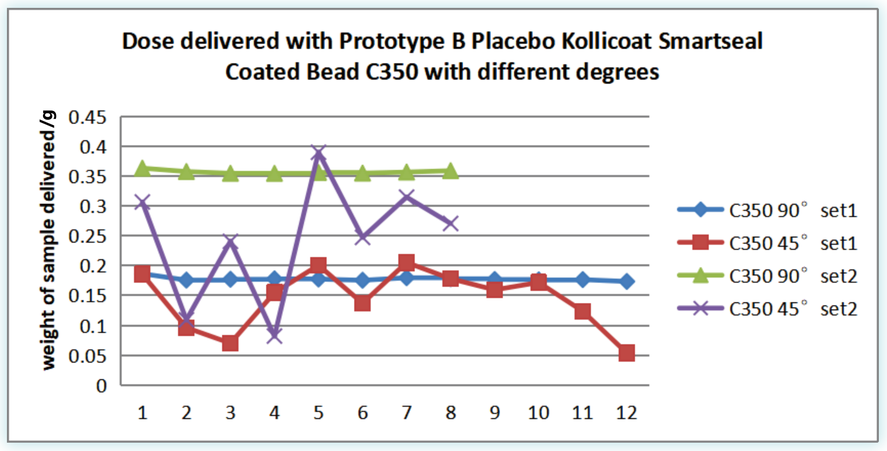


Figure 7

At 90 degrees, the device demonstrated good dosage delivery accuracy. However, at 45 degrees, the device was affected by the angle and thus the dosage was inconsistent, preventing accurate delivery of the drug. This was also seen in other sample studied.

CONCLUSION

Precise dosing of low powder masses can prove challenging, partly due to limitations in volumetric dosing technologies reliant on powder flowability. Successful consistent dose delivery of powders and granules via the Powdose device hinges on optimal flowability and a narrow particle size distribution. This study helped to recommend the device refinement necessary to ensure consistent and reliable dose delivery using the Powdose.

Reference:
[1] European Pharmacopoeia. 11th ed. Council of Europe; 2022.
[2] United States Pharmacopeial Convention. USP 36 Pt. 905. United States Pharmacopeial Convention.