DEVELOPMENT OF A DIRECT IN VESSEL AEROSOL COLLECTION APPARATUS FOR DISSOLUTION TESTING

Mårten Svensson[1], Lena Heintz[1], and Kjell Fransson[2].
[1]Emmace Consulting AB, Scheelevägen 22, 223 63 Lund, Sweden. [2]AB FIA, Medicon Village, Scheeletorget 1, 223 63 Lund, Sweden.

Drug Delivery to the Lungs, Volume 34, 2023 - Mårten Svensson et al.

EPAG European Pharmaceutical Aerosol Group www.epag.co.uk

AB FIA www.fia.se

EMMACE www.emmace.se

INTRODUCTION

Dissolution testing of inhaled drugs has received significant increased interest over the last ten years. However, a simple and standardised dissolution apparatus with discriminatory power is still not widely available to industry or academia. An aerosol collection apparatus was designed to capture particles directly into a liquid medium in a standard dissolution vessel, to avoid potential issues when using a filter for collection.

Representatives of member companies of the European Pharmaceutical Aerosol Group (EPAG), and its Dissolution Sub-Team decided to evaluate whether direct collection of an inhaled dose into a standard dissolution vessel could be possible. It was felt that this could provide a route to a simplified experimental setup, using familiar equipment, and avoiding generation of powder layering on a filter surface which could unduly influence the dissolution assessment.

EXPERIMENTAL METHODS AND MATERIALS

The custom apparatus is shown in Figure 1, and comprises an Andersen USP throat and pre-separator leading to a conical adaptor on the dissolution vessel. The adaptor is joined to a cylindrical inlet tube which has an array of nozzles, placed around 1 cm below the liquid surface (200 mL). Two nozzle types were evaluated with differing sized jets (“small” and “large”). An outlet filter was in place between the vessel and TrB III flow controller (AB Fia) / vacuum pump. Air flow was 60 lpm and all testing was at ambient temperature.

***Table 1**. Method details for the tests.*

Test	A	B	C
Inhaler	Flixotide Accuhaler (250 µg fluticasone propionate, batch FY5U, expire date 9/2023, two doses)	Flixotide Accuhaler (500 µg fluticasone propionate, batch WL7Y, expire date 10/2022, one dose)	Same as in Test A
Suction time (sec)	4	0.6	Same as in Test A
Type of dose capture	Direct in Vessel, small and large jets	Direct in Vessel, small jets	Membrane filter in modified ACI [1]
Surfactant (0.2% SDS) presence	After dosing	Before dosing	Same as in Test A
Media stirring	Paddle, 100 rpm	Magnetic stirrer, 300 rpm	Same as in Test A

***Figure 1**. Photos of the Direct in Vessel aerosol collection apparatus.*

RESULTS

Obtained drug amounts shown in Table 2. The amount dose collected for the dissolution assessment was significantly lower when using the Direct in Vessel approach in Test A. Most of the missing dose was recovered from the outlet filter.

Prior start of Test B, the effect from air suction time on drug on outlet filter was investigated (Figure 2). 0.6 sec was deemed acceptable and selected for Test B.

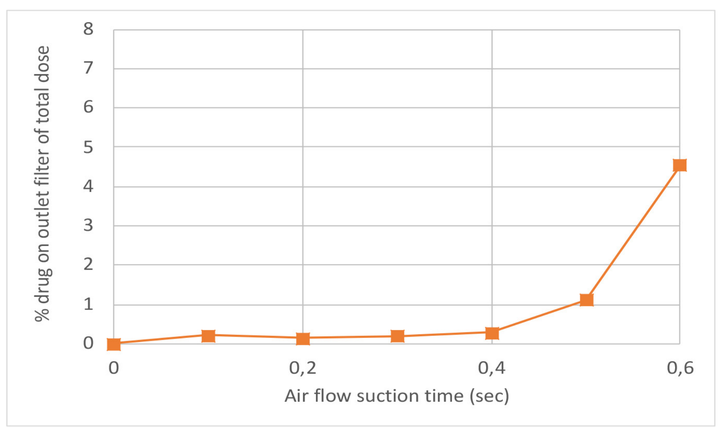


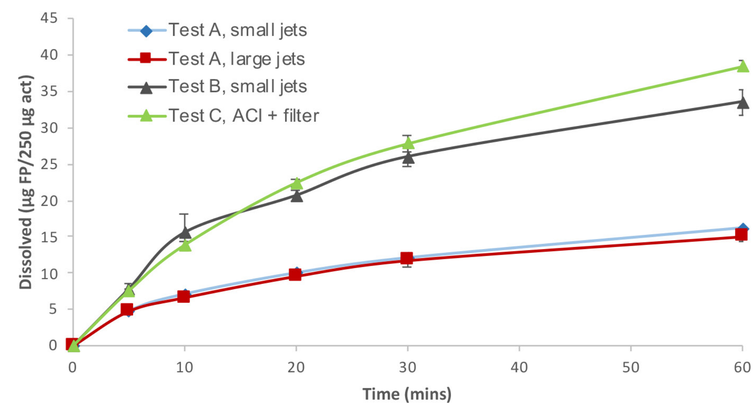
***Figure 2.** Amount drug (% of full dose) on outlet filter vs different air flow suction times.*

***Table 2**. Mean±SD. Drug recovery from the different tests.*

Test	Apparatus Configuration	Total Dissolution Recovery (µg)	Outlet Filter (µg)	Nozzle (µg)	Membrane Residue	Total Experimental Recovery (µg)	No of replic.
A	Direct in Vessel - Small Jets	19.0±2.6	20.1±1.4	6.5	N/A	45.6±1.2	4
A	Direct in Vessel - Large Jets	17.3±0.9	23.7±1.2	4.4	N/A	45.3±1.2	4
B	Direct in Vessel - Small Jets, SDS present in media during dosing	39.8±1.5	1.8±2.6	Not measured	N/A	41.6±1.4	2
C	Modified ACI (comparator)	43.5±1.8	N/A	N/A	3.2±0.2	46.7±1.9	3

The dissolution profiles, expressed as µg and as % of total dissolution recovery are shown in Figure 3.

In Figure 3 (upper), it is seen that a filter (Test C) for powder collection gave the highest recovery in the media. When using a shorter air suction time plus SDS in the media before dosing gave comparable recovery to the filter method. A longer (4 sec) suction time plus adding the SDS after dosing gave poor recovery. When normalised based on total dose recovered (Figure 3 (lower)) the dissolution rates are comparable for the different methods.



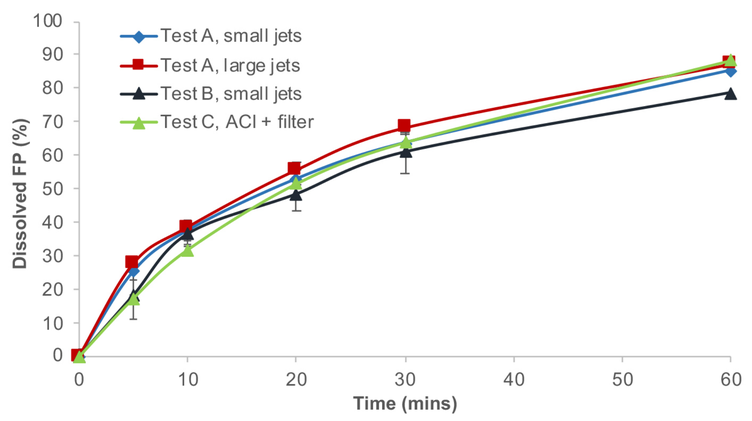


***Figure 3**. Mean±SD. Dissolution profiles obtained from the Tests in absolute mass (upper panel) terms, so is affected by aerosol dose collection efficiency.*

Lower panel shows the profiles normalised as a % of aerosol dose.

DISCUSSION

The major challenge with a Direct in Vessel approach is relatively poor aerosol dose capture by the liquid medium when no surfactant is present during dosing and 4 sec suction time was used. When surfactant was present in the media during dosing with a reduced suction time (0.6 sec) the dose collected in the media was comparable to the filter method.
Collection of the aerosol dose directly in a liquid medium for dissolution testing seems to be a feasible and alternative approach compared to the use of a filter substrate. This may allow a simplified experimental setup more closely coupled to a standard dissolution vessel (i.e. USP II), giving potential for automation and re-use of already available apparatuses.

CONCLUSIONS

In the presence of a surfactant in the liquid media during dosing and applying a short air pulse (0.6 sec) for dose actuation a proof of principle Direct in Vessel aerosol collection apparatus was successfully designed and assessed for dose capture and subsequent dissolution analysis. The Direct in Vessel method could be a simple and effective way to carry out dissolution measurements for inhaled products. but further characterization work will be needed to optimize the total dose capture.

ACKNOWLEDGEMENTS

This work was funded by EPAG, and the authors wish to thank past and present members of the EPAG Dissolution Sub-Team for their input and discussion: Joe Takher-Smith, Sara Poole, Eunice Costa, Andy Cooper, Per Bäckman, Frank Chambers, Gopi Kandasamy, Sim Bansal, Marc Kelly, Laura Matilainen, Per Gerde, Beatriz Fernandes, Flo Gower & Jim Clay.

Download the poster in pdf-format.

REFERENCE

[1] May, S., Jensen, B., Weiler, C., Wolkenhauer, M., Schneider, M., & Lehr, C.-M. (2014). Dissolution testing of powders for inhalation: Influence of particle deposition and modeling of dissolution profiles. Pharmaceutical Research, 31(11), 3211–3224.