NEAR-ORIFICE PDA MEASUREMENTS AND ATOMISATION MECHANISM OF A PHARMACEUTICAL PRESSURISED METERED DOSE INHALER

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Abstract

A comprehensive analytical and PDA and imaging survey of the aerosol plumes produced by a pressurised metered dose inhaler, pMDI using placebo and active formulations based on the HFA227 propellant is in progress. The work described here concentrates on, what the authors believe, are the first set of PDA measurements in the near-orifice region of a pharmaceutical pMDI. The axial and radial velocity components and the arithmetic and Sauter mean diameter profiles are presented and discussed in a measurement plane X/D of 6.2 relative to the nozzle orifice diameter. The experimental data are compared with numerical data obtained from a modified version of the phenomenological model of the propellant flow in the pMDI valve due to Fletcher (1975) and Clark (1991) in order to examine the underlying mechanisms of pMDI valve flow and spray droplet formation.

Introduction

A modest number of investigations have been carried out to document the characteristics of sprays produced by atomisation mechanisms involving flash evaporation. One notable early exception being the work by Solomon *et al*, (1985), who measured the velocity and drop size distribution of propellant P11 sprays in still, ambient air using Laser Doppler Anemometry (LDA), slide impaction and flash photography. More recently, the switch from CFCs to more ozone-friendly propellants and FDA proposals for improved characterisation of medical aerosols have renewed interest in these sprays. Building on early work by Fletcher (1975), Clark (1991, 1996) developed a qualitative description of the main events inside the valve stem of a pMDI actuator as well as a phenomenological model leading to predictions of transient mass flow rates of propellant. Dunbar (1996, 1997[a]) used Phase Doppler Anemometry (PDA) and high-speed photography to study aerosol plumes produced by a pMDI actuator. Placebo formulations based on propellant HFC134 and mixtures of propellants P11/P12 were tested as well as an active formulation with P11/P12 as the propellant. The following spray characteristics have thus far been identified:

- The spray issuing from a pMDI is highly unsteady and three-dimensional and is characterised by high initial drop velocities with large spatial gradients and complex temporal behaviour. Drop sizes are small, typically less than 10 microns and the mean spray cone angle is 10-12 degrees.
- High-speed photography studies suggested that the spray is pre-atomised inside the pMDI valve stem. Internal flash evaporation is understood to be the main primary atomisation mechanism in pMDI aerosols, which involves a droplet formation mechanism that is akin to airblast atomisers.
- Temporal analysis shows that the spray initially consists of a small number of larger, faster moving drops with a large number of smaller, slower moving drops produced during the second half of the actuation.
- Due to the small size of the spray droplets, turbulent momentum, heat and mass transfer govern the far field characteristics of these sprays. Secondary atomisation processes such as coalescence and breakup are not believed to play a major part in spray development.

These findings were based on examination of high-speed images of the near-orifice flow and far field, $x/D \geq 50$, LDA and PDA data. Near-orifice measurements, $x/D \leq 20$, have so far failed due to PDA signal drop-out or unacceptably low data validation rates. Dunbar attributed these problems to violation of the maximum number concentration limit for his instrumentation and/or excessively high vapour mass fractions resulting in beam steering. Due to the comparatively modest data rates, temporal data had to be presented in time windows of 20 milliseconds width. With such a discretisation, 8-10 time windows describe a pMDI actuation event of total duration 0.15-0.2 seconds. This is insufficient to capture all the rapid transients, in particular, those during

the start-up phase, when high-speed photography shows that substantial quantities of much larger droplets in the size range 30-60 microns are formed.

Experimental Procedure

The design and construction of the two component high power, high resolution LDA/PDA transmission system has been well documented, Wigley (1999). The configuration for this application is given in Table 1.

Transmitter	Radial velocity component	Axial velocity component
Wavelength	514 nm	488 nm
Power - Total	450 mW	250 mW
Beam Separation	50 mm	50 mm
Beam Width	5.0 mm	5.0 mm
Focal Length	300 mm	300 mm
Measurement Volume Diameter	40 µm	37 µm
Fringe Spacing	3.10 µm	2.94 µm
Number of Fringes	13	13
Light Polarization	Parallel to Fringes	Parallel to Fringes
Receiver (Dantec 57X10)		
Scattering Angle	70 degrees	
Lens Focal Length	310 mm	
Measurement Volume Length	110 µm	
Aperture / Max. Dropsize	2.0 mm / 60 µm	
Phase factor	8.80 degrees/µm	
Processor (Dantec Enhanced 58N50)		
PM High Voltage	824 V	
Bandwidth / Gain	45 MHz / Low	
Validation		
Signal Level / Velocity	Yes	
Validation Level	0 dB	
Diameter / Spherical	Yes	
Phase error	10 degrees	
Spherical Deviation	10 %	

Table 1. PDA parameters and Specification

The pMDI actuators were mounted in the clamping block of an automated shake/fire robot. It incorporated a rotation stage and pneumatic hammer to strike the propellant canister. A microphone recorded the strike and produced an acoustic trigger to identify the start of each actuator firing. To avoid excessive cooling of the actuator nozzle, due to the flash evaporation of the propellant a 10 second delay was introduced between one firing and the subsequent shake prior to the next actuation.

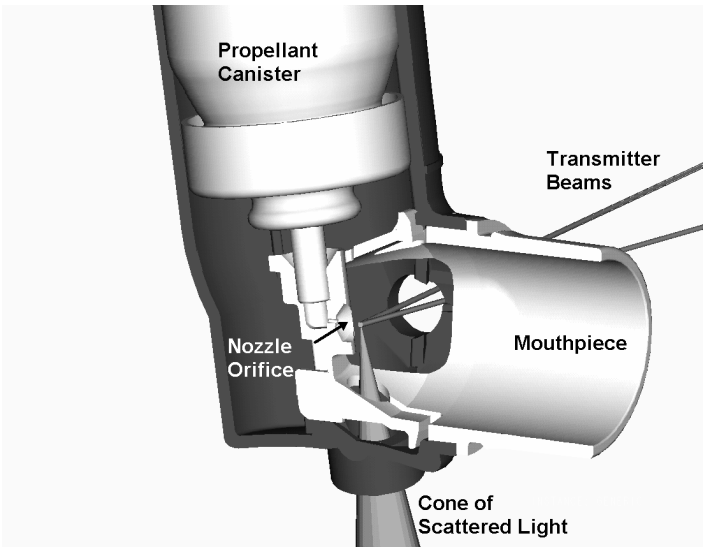

Figure 1 Schematic of pMDI actuator with windows in the mouthpiece for optical access

The orientation of the spray was dependent on the study performed. In normal operation the actuator is held as shown in Figure 1 and the spray is fired in the horizontal direction. This orientation was used for measurement surveys in the far-field region of the spray downstream from the pMDI mouthpiece. Measurement surveys in the near-orifice region of the actuator could only be carried out by rotating the robot to fire vertically downwards. This was due to the requirement of matching the optical paths, for the entry of the transmitted laser beams and for the exit of the full cone of scattered light which were in the horizontal plane, to the windows in the actuator mouthpiece.

Preliminary trials established that it was necessary to collect data from 10 shots fired at each measurement point. This was in order to:- (1) acquire a sufficiently large number of samples in the less dense parts of the spray to compute reliable average values of mean and rms droplet velocity and droplet size and (2) acquire a significant number of actuations per position on the dense spray axis. Collecting data from a fixed number of actuations makes it much easier to compare the distribution of data samples across the spray. It was found possible to make spray plume measurement traverses with good shot-to-shot and can-to-can repeatability. Dunbar (1996) used a similar number of shots in his PDA experiments.

PDA Results and Discussion

Near-orifice data of the simultaneous axial and radial velocity and dropsize were collected along a horizontal traverse at an axial distance of 2.6 mm downstream from the actuator orifice of diameter 0.4 mm. The traverse scan was limited, to eight positions with a step size of 0.2 mm, by the 5 mm diameter windows in the mouthpiece. Velocity and dropsize data were first displayed as discrete scatter plots for the time history of each individual sample relative to the actuator acoustic trigger. These data were then time bin averaged, over sector sizes of 2 and 4 milliseconds, to produce time varying mean profiles of axial and radial velocity, dropsize and sample number. Examples of these data are shown in Figures 2 and 3 with the scan data identified by position number. The location of the spray axis was taken as that position which produced the maximum mean axial velocity.

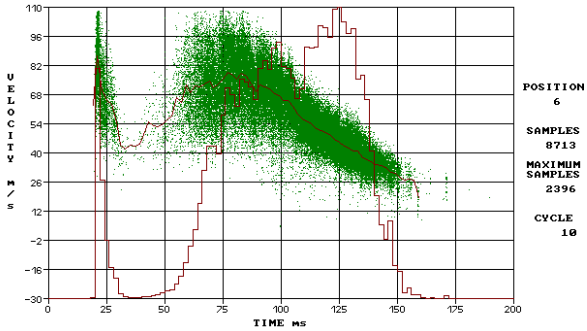

Figure 2 Discrete velocity data and mean profiles

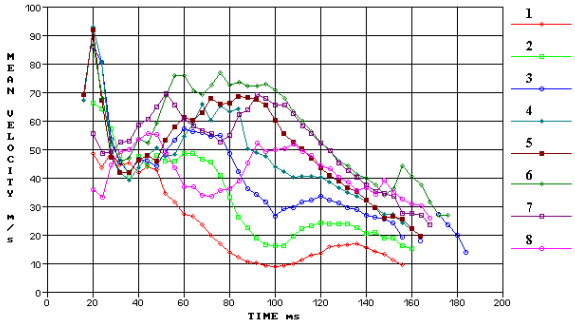

Figure 3 Mean axial profiles across the spray

The discrete axial velocity data shown in Figure 2 are for position 6. The time bin averages for the mean axial velocity and sample distribution histogram was taken as 2 milliseconds. With 10 shots nearly 78,000 samples were collected and the normalised sample histogram has a peak of 2396 samples in the 2 millisecond time bin at 125 milliseconds. This equates to a mean data rate of 120 KHz. However, instantaneous data rates were sometimes in excess of 200 KHz and the maximum data throughput of the signal processor. Although these sprays have a very high droplet number per unit volume they are not optically dense due to the high very high degree of atomization and small dropsize. This plot highlights the temporal development of the spray. Starting at 16 milliseconds after the acoustic trigger there is a short pulse of spray lasting for 10 milliseconds with a peak mean axial velocity of 90 metres/second. After this the sample number falls dramatically before the main event occurs starting at nominally 50 milliseconds. The mean axial velocity and sample number per time bin are both seen to increase although their respective peaks are not correlated.

Presentation of the time resolved data in Figure 3 has used 4 millisecond time bins to yield excellent statistical representation of the events associated with the pMDI actuation event. During the first 16-20 milliseconds of the traces in Figure 3 the largest velocities occur at measurement stations 4-6, whereas during the final stages, corresponding to maximum sample numbers, the highest velocities occur at stations 6-7. Furthermore the profiles are not symmetrical about position 6. Measurements of the cross flow or radial velocity component reveal that initially there is a distinct bias to the spray. These results, shown in Figure 4, indicate deviations from the horizontal during the course of an actuation event. It must be remembered that the PDA system measures the true vertical and horizontal velocity components whereas the actuator may not necessarily

be aligned to produce a horizontal spray. Nevertheless, the radial flow profile for position 6 with the maximum axial mean velocities demonstrates a near zero radial flow component for the time period up to 90 milliseconds.

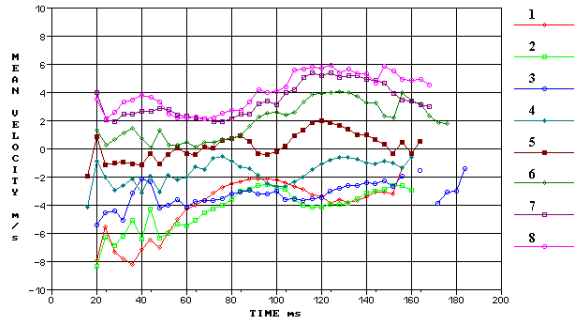

Figure 4 Mean radial profiles across the spray

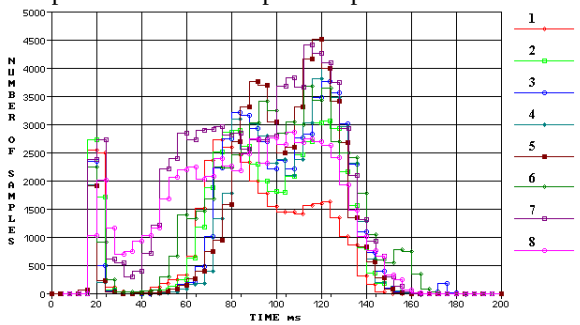

Figure 5 Sample distribution profiles across the spray

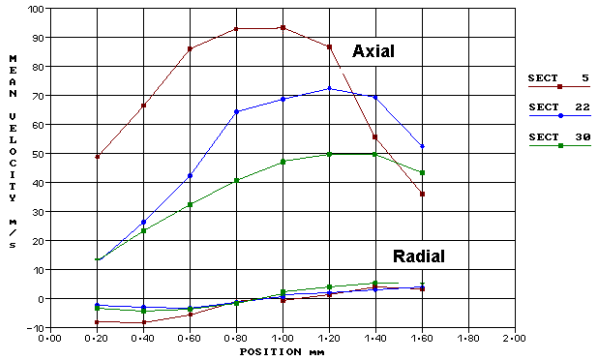

Figure 6 Spatial variation of mean velocity profiles across the spray as a function of time

This asymmetry is also seen in the sample number histograms shown in Figure 5 where, in the spray after the initial pulse, relatively large sample counts per time bin are found. The asymmetry is best illustrated by plotting the spatial variation of the axial and radial droplet velocity across the scan as a function of time. Three specific times, 20, 90 and 120 milliseconds are shown in Figure 6 with the time bin sector number representative of the two maximum velocity peaks and maximum sample count.

The degree of atomization of the liquid propellant is very high with small dropsizes and a variation in the mean droplet diameter, D_{10}, of generally between 2 and 5 microns, Figure 7. The corresponding profiles for the Sauter mean diameter, D_{32}, in Figure 8 reveal a different character to the spray. Sprays comprising of a very large fraction of small droplets but containing a small fraction of large droplets will show widely different values for the dropsize mean values represented by D_{10} and D_{32}. These Figures demonstrate this, particularly, immediately after the initial spray pulse and towards the end of the actuation. Again the asymmetry in the spray development is seen with large droplets being recorded at positions 1 and 2 starting at 80 milliseconds through to the end of the spray.

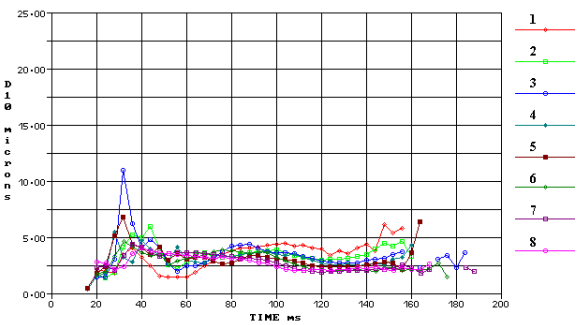

Figure 7 Mean D_{10} dropsize profiles across the spray

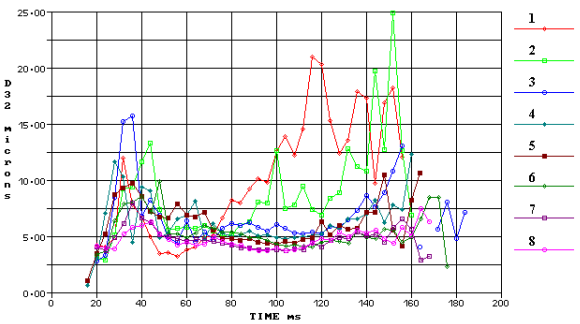

Figure 8 Mean D_{32} dropsize profiles across the spray

Phenomenological Model of Atomisation Mechanism

Numerical predictions of the two-phase mixture velocity and droplet size are based on a quasi-steady, homogeneous, adiabatic, frozen flow model of the propellant inside the pMDI actuator valve (Fletcher, 1975; Clark, 1991). The actuator valve comprises of a system of three spaces; the metering chamber, the valve stem and ambient atmosphere, which are connected by the valve orifice and the actuator orifice, respectively. Comparisons of predicted and measured temporal profiles of mean propellant velocity and droplet size in the near-orifice region are given in Figures 9 and 10. Temporal profiles, denoted by PDA were drawn using data from the spray core corresponding to where the highest droplet velocities were found.

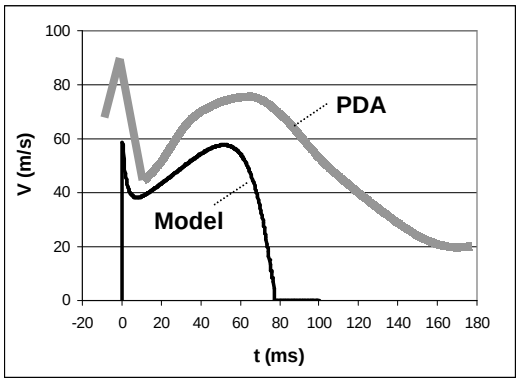

Figure 9: Temporal profiles of propellant velocity

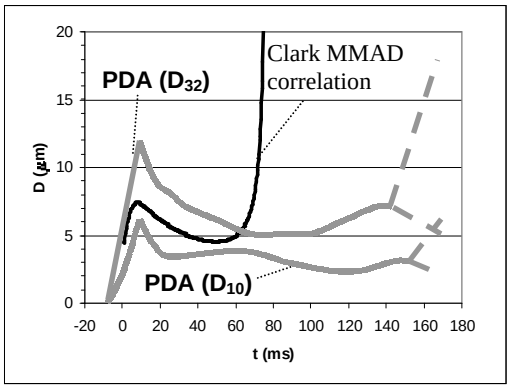

Figure 10: Temporal profiles of mean drop size

According to the model, the initial velocity spike is associated with subsonic, two-phase flow with high vapour mass fraction through the actuator orifice due to rapid initial evaporation of the propellant mixture. The imbalance in the valve stem between the mass flow rates of incoming, liquid-rich, and outgoing, vapour-rich, propellant mixture causes the internal pressure to rise. Propellant evaporation is inhibited and the vapour mass fraction reduces. This strongly reduces the speed of sound of the two-phase mixture; consequently, the flow at the actuator orifice chokes. The spray velocity starts to reduce and reaches a minimum. Subsequently, the pressure rise in the valve stem causes a reduction of the incoming mass flow rate from the metering chamber below the mass flow rate discharged through the actuator orifice. This increases propellant evaporation and the spray velocity starts to pick up again until a second velocity maximum is reached. At this stage the model indicates that the changes in valve stem conditions cause the flow in the actuator orifice returns to subsonic conditions. The spray velocity now starts to decay progressively as the propellant runs out. Discrepancies between the model predictions and PDA data are attributable to non-adiabatic flow due to heat transfer effects. In particular, the model predicts that the pressure inside the valve becomes equal to the ambient pressure due to adiabatic cooling of the mixture after about 80 milliseconds. At this stage the predictions suggest that the flow should stop. The PDA data show that, during the final 60-80 milliseconds of the actuation event, the remnants of propellant in the metering valve and valve stem slowly evaporate.

The initial rapid changes in conditions strongly affect the flow regime inside and droplet production mechanism just outside the valve stem. A comparison of PDA drop size data (D_{10} and D_{32}) with the results of an empirical drop size correlation for mass median aerodynamic diameter (MMAD) developed by Clark (1991) is shown in Figure 10. The droplet size is first predicted to increase rapidly in response to choking of the actuator orifice. The correlation subsequently predicts a gradual reduction of the droplet size as the vapour mass fraction increases again, followed by a rapid rise after about 70ms. At this stage the pressure difference across the actuator orifice becomes small and the empirical drop size correlation ceases to be valid as.

Conclusion

Spray characteristics in the near-orifice region, x/D = 6.2, of a pharmaceutical pressurised metered dose inhaler were studied using PDA. Results showed that a highly pre-atomised spray with typical mean drop size D_{10} between 2 and 5 microns emerges from the actuator orifice. The spray exhibits a complex temporal behaviour including significant transient movement normal to the main spray direction. Good agreement during the first 70 milliseconds of the actuation event between measured velocities and predicted trends of a phenomenological propellant flow model through the actuator valve confirms its thermodynamic assumptions and the associated pre-atomisation mechanism. Discrepancies are attributable to heat transfer effects.

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Appendix: Functionality of Phenomenological Model of Aerosol Plume Source