

Development of a theoretical model to predict pMDI spray force, using alternative propellant systems**Barzin Gavatash¹, Andy Cooper², Sarah Dexter², Chris Blatchford² & Henk Versteeg¹**¹Loughborough University, Epinal Way, Loughborough, LE11 2TL, United Kingdom²3M United Kingdom PLC, Charnwood Campus, 10 Bakewell Road, Loughborough, LE11 5RB, United Kingdom**Summary**

Continued success in the treatment of asthma and COPD requires new pMDI propellants for delivering aerosols with good patient comfort and acceptable levels of oral cavity deposition. The purpose of this work is to develop a theoretical model capable of predicting pMDI spray force as a function of metering valve geometric parameters and different propellant systems: HFA134a, HFA227ea and HFA152a. Such theoretical tool can be used in combination with lab-based measurements for device characterisation and potentially to reduce the number of experimental trials. The outcome of the model is compared against measurements of plume force with Copley Scientific Spray Force Tester SFT 1000. Results suggest that the size of the spray orifice has a significant direct effect on the spray force. We have also observed HFA134a and HFA152a generates similar magnitude of spray force and velocity where HFA227ea generates the lowest velocity and force values. These findings could potentially mean HFA152a sprays are expected to show similar levels of mouth-throat deposition to HFA134a sprays rather than HFA227ea sprays.

Key Message

Predicted and measured values suggest that spray orifice size had a significant effect on metered dose inhaler spray force. It was also observed that HFA152a and HFA134a show similar spray force values where HFA227ea generates the lowest force values.

1. Introduction

Kigali 2016 amendment of Montreal Protocol has delivered international agreement to phase out hydrofluorocarbons on the grounds of their high global warming potential. Replacements for pressurised metered dose inhaler (pMDI) propellants HFA134a and HFA227ea will need to be developed for inhalation therapies. Recently HFA152a has received attention as an alternative propellant to be used in pMDI [^{1, 3, 4}] due to its much lower global warming potential (around 124) compared with HFA134a and HFA227ea (around 1400 and 3200 respectively). However, the feasibility of formulating pMDIs using HFA152a is still under rigorous investigation mainly from a safety and patient acceptability standpoint [¹]. One important plume characteristic which influences patient acceptability is maximum spray force which also directly correlates with oropharyngeal deposition [^{1, 5, 6}]. Therefore, the aim of this paper is to develop a theoretical model capable of predicting pMDI spray force as a function of metering valve geometric parameters and different propellant systems: HFA134a, HFA227ea and HFA152a. In past work [^{2, 9}], results with two existing propellants have been validated. The present work includes mathematical predictions and experimental validation of spray force for proposed alternative propellant HFA152a with low global warming potential. Such theoretical tool can be also useful to minimise number of trials when it comes to pMDI device design/characterisation. We also compare model outcomes for different spray orifice sizes and propellants against measured values to increase confidence of the modelling activity.

2. Mathematical model

Prediction of pMDI spray force requires calculation of two-phase propellant mass flow rate and velocity inside twin-orifice system of pMDI [²]. Such model was originally developed by Fletcher [⁷] and Clark [⁸] and has been recently improved, validated and comprehensively discussed by Gavatash et al. [^{2, 9, 10}]. Here we briefly discuss the key components of the model and underlying equations. Therefore, the reader is advised to refer to the references for further details. Our internal flow model is quasi-steady and assumes the propellant expansion is adiabatic and involves thermodynamic and thermal equilibrium between the propellant liquid and vapour phase, inside the metering and expansion chambers. The two-phase propellant flow through valve and spray orifices in a pMDI is evaluated with the homogeneous frozen model (HFM), which assumes that no evaporation takes place along the flow path through the orifices and the flow is choked for almost 90% of the actuation time. The spray force, F , can be calculated using one-dimension steady momentum equation:

$$F = GAV_{no}$$

1

Where $A = \pi D_{so}^2/4$ (m^2) is the spray orifice cross section area and $G = \dot{m}/A$ (kgm^2/s) is the two-phase propellant mass flux through spray orifice which can be calculated using the following expression [²]:

$$G = C_d \left(\frac{p_0}{x_0 v_{g,0}} \frac{2\eta^{\frac{2}{\gamma}}}{\left[\left(\frac{1-x_0}{x_0} \right) \left(\frac{v_{l,0}}{v_{g,0}} \right) \eta^{\frac{1}{\gamma}} + 1 \right]^2} \left[\left(\frac{1-x_0}{x_0} \right) \left(\frac{v_{l,0}}{v_{g,0}} \right) (1-\eta) + \frac{\gamma}{\gamma-1} \left(1 - \eta^{\frac{\gamma-1}{\gamma}} \right) \right] \right)^{\frac{1}{2}} \quad 2$$

In equation 2, subscript 0 denotes the flow condition in the upstream reservoir (expansion chamber) and subscripts g and l denote the gas phase and liquid phase thermodynamic properties, respectively. γ (-) is the propellant heat capacity ratio, v (m^3/kg) is the specific volume and p (Pa) is the saturated vapour pressure. x (-) denotes the two-phase flow quality and C_d (-) is the discharge coefficient. Finally, $\eta = p_{so}/p_0$ (-), denoting the ratio of spray orifice pressure to upstream reservoir pressure. Due to the choked nature of the emitted two-phase flow from spray orifice, p_{so} is generally higher than the ambient downstream pressure. This pressure further accelerates the flow in near-orifice region. Corresponding velocity in near-orifice region can be calculated using equation 3, which is one-dimensional axial momentum balance in a diverging control volume close to the spray [2]:

$$V_{no} = G\bar{v} + \frac{p_{so} - p_{amb}}{G} \quad 3$$

Where p_{amb} is the ambient pressure and \bar{v} is the average two-phase flow specific volume at the spray orifice exit. Assuming isentropic expansion of the propellant vapour phase inside the spray orifice, \bar{v} reads as follows [2]:

$$\bar{v} = \eta^{-\frac{1}{\gamma}} x_0 v_{g,0} \left[\left(\frac{1-x_0}{x_0} \right) \left(\frac{v_{l,0}}{v_{g,0}} \right) \eta^{\frac{1}{\gamma}} + 1 \right] \quad 4$$

3. Experimental set-up

Measurements are performed with a commercial spray force tester instrument (SFT 1000, Copley Scientific), as shown in Figure 1. The sledge which holds the pMDI is positioned such that the mouthpiece edge is 50mm from the load cell. Nine configurations of placebo inhalers, configured as per Table 1, are assessed in triplicate. The load cell records the maximum force observed during the spray event.

Parameter	Value			Parameter	Value		
Metering valve volume (μ l)	63			Discharge coefficient (-)	0.6 ^[2]		
Expansion chamber volume (μ l)	13			Ambient temperature (K)	295		
Valve orifice diameter (mm)	0.6 ^[2]			Ambient pressure (Pa)	101300 Pa		
Spray orifice diameter (mm)	0.3	0.4	0.5	Propellant (HFA)	134a	227ea	152a

Table 1 – Experimental and modelling parameters



Figure 1 – Experimental setup (SFT 1000)

4. Result and discussion

4.1 Spray velocity and mass flowrate

Figure 2 shows the mass flow rate through the 0.3 mm spray orifice, predicted for three propellants as a function of actuation time. Initially, propellant starts to flow from the metering chamber to the expansion chamber of the pMDI, causing a rapid rise of the pressure in the expansion chamber and the spray mass flow rate. During this phase, the mass flow rate entering the expansion chamber is greater than the mass flow rate exiting this space. Hence, propellant evaporation in the expansion chamber becomes inhibited, which leads to a greater fraction of liquid in the discharged mixture. As a consequence, the average density of the emitted mixture increases and the mass flow rate through spray orifice rises up to a maximum value. After the maximum, the mass flow rate leaving the expansion chamber through the spray orifice becomes larger than the mass flow rate entering from the metering chamber. Evaporation increases, and the mass flow rate decreases continuously, until the discharge concludes. It can be observed that the peak mass flow rates are approximately similar for all three propellants considered in this study. It should be noted that similar temporal trends are observed for 0.4 mm and 0.5 mm spray orifice diameter cases with different mass flow rate magnitude and spray duration.

Figure 3 shows the predicted near-orifice spray velocity of the 0.3 mm spray orifice. Results suggest that the velocity almost instantaneously rises which corresponds to the discharge of high quality vapour/liquid propellant mixture through the spray orifice. After this point a subsequent fall in the velocity is observed at around 10 ms after the actuation time. This time corresponds to when the peak mass flow rate occurs. From this minimum point, velocity almost linearly increases as a result of expansion chamber emptying, until it reaches a second maximum. Finally, the mass in the chambers depletes completely and the velocity sharply decays until it reaches zero.

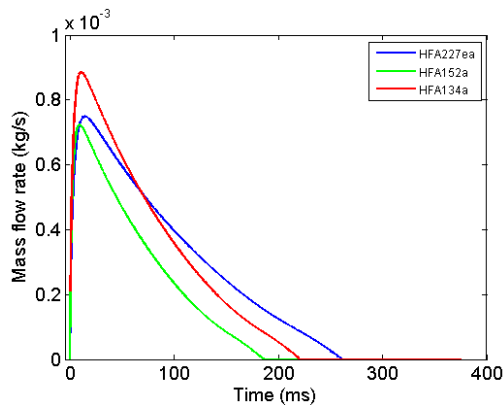


Figure 2 – Time dependent average mass flow rate of two-phase propellant flow issued from the spray orifice ($D_{so}=0.3$ mm)

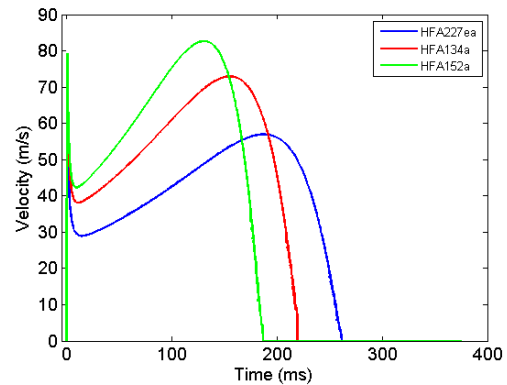


Figure 3 – Time dependent spray velocity at the exit plane of spray orifice ($D_{so}=0.3$ mm)

Comparison of the traces suggests that HFA152a shows the highest spray velocity whereas HFA227ea has the lowest velocity amongst the three propellants. Such trend can be best described by investigating the propellants vapour pressure as the main driving force of the flow, and density as the main opposing parameter to acceleration. Over a typical range of pMDI operating temperature of around -20 to 20 °C in this study, saturated vapour pressure of HFA152a and HFA134a are very similar in terms of magnitude (less than 8% difference), with HFA152a being slightly lower. However, the liquid density of HFA152a is around 25% less than the one of HFA134a. Therefore, propellant pressure is used to accelerate a lighter mass which overall results in higher velocity of HFA152a compared with HFA134a.

4.2 Spray force

Figure 4 shows the temporal behaviour of spray force for 0.3 mm orifice diameter. It can be observed that the force initially rises to a maximum and then more gradually decreases until the spray event finishes. This trend in time is very similar to the previous temporal force measurements^[5, 8]. The results also suggest that the maximum force is experienced during the filling stage of the expansion chamber where liquid-rich two-phase propellant flow exits the spray orifice. Figure 5 shows comparison of predicted and measured spray force for different propellants and different spray orifice diameters. The predicted force values are averaged over the duration which 95% of pMDI propellant mass is emitted. It can be observed that the trend in variation of spray force with respect to propellant and orifice diameter are very well captured by our model prediction. Data shows that for any propellant, increase in spray orifice diameter results in a significant increase in spray force. This is mainly due to release of more mass per unit time as orifice diameter increases. Amongst the three propellants considered in this study, for any orifice diameter, HFA227ea spray produces the smallest force. The generated force by HFA134a and HFA152a propellants appears to be very similar in magnitude with HFA134a being slightly higher. When compared with measured values, the model outcomes are predicted within the correct order of magnitude.

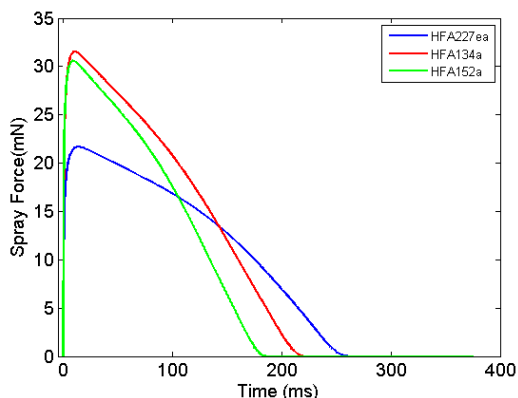


Figure 4 – Time dependent spray force at the exit plane of spray orifice ($D_{so} = 0.3$ mm)

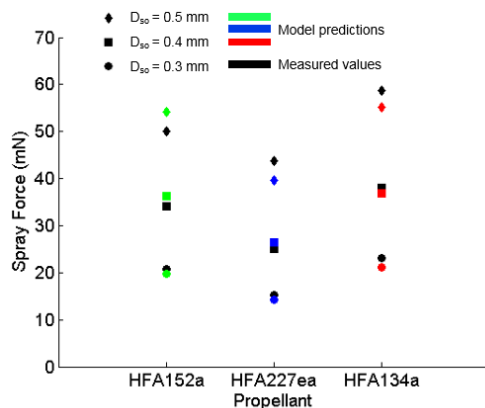


Figure 5 – Comparison of predicted and measured plume force for different propellant systems and orifice sizes

Conclusion

In this paper we have reported the findings of a theoretical model, capable of predicting spray force as function of metering valve geometric parameters and various propellant systems. Such theoretical tool can be used in combination with lab-based measurements for device characterisation and potentially to reduce the number of experimental trials. Amongst the studied propellants, our theoretical predictions suggest that the spray velocity is lowest for HFA227ea whereas it is relatively similar for HFA134a and HFA152a, being slightly higher for HFA152a. Our theoretical and measured force values demonstrate that orifice size is the most influential factor on, and directly correlates with spray force. Data also suggest that HFA227ea has the lowest force where HFA134a and HFA152a exhibit similar force values for any particular orifice size. Assuming there is a direct correlation between spray force and oropharyngeal deposition^[1, 5, 6], these findings could potentially mean HFA152a sprays are expected to show similar levels of mouth-throat deposition to HFA134a sprays. However further investigations are required to confirm such hypothesis.

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