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The effect of reduction of propellant mass fraction on the injection profile of metered dose inhalers

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ABSTRACT

In order to provide an improved understanding of the flow in pressurized-metered dose inhalers (pMDIs), especially monitoring the output temperature and mass flow rate to obtain maximum atomization efficiency from the available energy, a numerical model for a two phases, multi-component compressible flow in a pressurized-metered dose inhaler is presented and validated. It is suitable for testing with various formulations and different geometries for a range of pMDI devices. We validated the model against available data in the literature for a single component HFA 134a propellant, and then investigated the response of the model to other formulations containing non-volatile components. Further validation is obtained by an experiment using the dual beam method which acquired the actuation flow properties such as spray velocity and duration. The deviation of the numerical predictions for the peak exit velocity against the experimental results is 5.3% and that for effective spray duration 5.0%. From the numerical and experimental results, it is found that for the formulations with the mass fraction of HFA 134a > 80%, the effective spray duration of the pMDI is around 0.1 s. Furthermore the droplet peak exit velocity at the axial station $x = 25$ mm from the actuation nozzle decreases from 20 to 15 m/s with the reduction of the propellant (HFA 134a) from 95%. Formulations with the mass fraction of HFA 134a below 80% produce poor quality spray which is indicated from the unsteady peak exit velocity, changeable spray number density in each experimental test, and numerical simulations also confirmed the non-viability of this condition.

1. Introduction

Pressurized-metered dose inhalers (pMDIs) are widely used pharmaceutical devices designed to deliver aerosolized medication deep into the lung (Finlay, 2002). To obtain a single dose, a consumer first actuates the device by squeezing the canister into the canister casing, while simultaneously inhaling via the casing mouthpiece. Newman (2005) presents an overview of pMDI design. When a pMDI is actuated, a pressurized mixture of medication and propellant is forced out of the canister through the metering chamber (MC) and expansion chamber (EC), specially designed to ensure consistent dosing throughout the life of the device. As the mixture passes through the expansion chamber, the pressure is reduced and the propellant begins to boil. Upon leaving the expansion chamber via the nozzle, the propellant forms droplets together with the drug particles or droplets producing a spray suitable for inhalation by the consumer. This basic design remained unchanged from the introduction of pMDIs in 1956 until a switch from chlorofluorocarbon (CFC) to hydrofluoroalkane-based (HFA) propellants began in the late 1990s. The emitted spray is transient, unsteady, turbulent, three-dimensional, and multiphase.

In recent years, several researchers have attempted to use computational fluid dynamics (CFD) to model air flow as well as the transport and deposition of aerosols in the human respiratory system. Farkas et al. (2006), Jin et al. (2007), Takano et al. (2006) and Kleinstreuer et al. (2007) simulated the air flow with particle transport and tracked the releasing particles within the calculated flow domain. Their results indicated the essential role of spray velocity initial conditions on simulating delivery of pharmaceutical aerosols in the respiratory system. For flashing propellant systems, of which pMDIs are an important device class, specification of these initial conditions is problematic.

Few works have appeared in the published literature in which researchers have attempted to characterized pMDI sprays actuations experimentally. Hochrainer et al. (2005) compared the spray duration and velocity of a number of CFC-and HFA-propelled pMDIs delivering different medications. The mean aerosol velocity was reported at a distance of 10 cm from the nozzle. Three medical formulations (ipratropium bromide, ipratropium bromide + fenoterol, and fenterol), were tested in both HFA- and CFC-propelled devices. In these cases, the average velocity of each of the HFA-propelled

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Nomenclature

A	cross-section area (m^2)
$c_{p/v}$	specific heat capacity at constant pressure/volume (J/(kg K))
C_d	discharge coefficient (−)
f	vapour mass fraction (vapour/gas mixture ratio) (−)
h	specific enthalpy (J/kg)
h_{fg}	latent energy of evaporation (J/kg)
H	enthalpy (J)
m	mass (kg)
$\dot{m}$	mass flow rate (kg/s)
M	molecular weight (kg/mol)
Ma	Mach number (−)
p	pressure (Pa)
q	quality of fluid (gas/mixture mass fraction) (−)
t	time (second)
T	temperature (K)
u	axial velocity (m/s)

Greek symbols

ρ	density (kg/m^3)
φ	volume fraction (−)

Subscripts

a	air
atm	atmosphere
b	background
c	critical
ds	downstream
ec	expansion chamber
g	gas
l	liquid
m	mixture
mc	metering chamber
P	propellant
r	relatively
t	nozzle throat
T	total
us	upstream

Superscripts

n	new time level
o	old time level
*	critical value

Universal constant

R	universal gas constant (8.314 (J/(mol K)))

pMDIs was always less than half the velocity of the corresponding CFC-propelled pMDI.

One detailed study of flash evaporation specifically in pMDIs has been conducted by Clark (1991), who attempted experiments to characterize the spray issued from a pMDI for various formulations in terms of spray mass flow rates, peak velocities, temperature, initial drop sizes and pressure variations in the MC and EC, and also developed a theoretical program for the single component flow to predict the above parameters. A range of peak exit velocities between 35 and 70 m/s were obtained at a distance of 30 mm from the actuator orifice, for propellant-134a with different orifice diameter ratios.

Dunbar (1996) provided a comprehensive theoretical and experimental analysis of the pMDI spray. They simulated the actuation flow with the single component numerical model, which indicates the multi-component actuation flow is required further study. They made experimental measurements at discrete points in the flow-field using phase-Doppler particle analysis (PDPA), which allowed droplet velocity, droplet size, and spray concentration to be measured. For the actuator orifice diameter of 0.5 mm, the axial peak exit velocity of the droplets 60 m/s was obtained at a distance of 25 mm from the actuator orifice and 15 m/s at 100 mm, with the spray duration of 0.195 s.

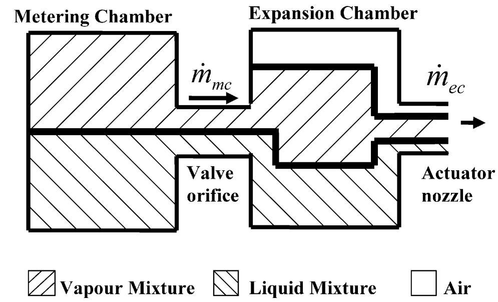

Fig. 1. Simplified actuation flow model.

The direct objectives of the current work are to study the process of flashing atomization and dispersion, with a view to supporting the development of devices to deliver nicotine based solution via an aerosol that mimics the action of smoking. Preliminary findings suggest that the nicotine formulations have different volatility characteristics, and hence there is a need to investigate the multi-component two-phase flow characteristics of flashing flow, typically found in pMDIs with the aim of optimizing the process to provide very fine atomization, and to evaluate the effect of different formulations on the spray characteristics for a typical pMDI geometry.

Here, spray velocities and duration were measured using the dual laser method (Dyakowski and Williams, 1993), which utilizes the well known cross-correlation technique. Measurements were performed using HFA-propelled pMDIs, and statistical comparisons were made to study variations in performance with a number of actuations as well as for different formulations (especially with different propellant mass fraction) actuated using a single pMDI discharging into quiescent air at normal temperature and pressure.

Results of this work will be particularly useful for future researchers seeking to simulate droplet dispersion and deposition in respiratory system as well as to help validate detailed simulations of the entire pMDI spray process.

2. Methods

2.1. Mathematical modeling of a pMDI

This work is based on an earlier model, for the single component actuation flow developed by Dunbar (1996). We have improved some of the multiphase flow assumptions and added multi-component two-phase flow functionality of flashing flow as detailed in Appendix. A simplified actuation flow model is shown as Fig. 1. The geometries of the pMDI are obtained from Dunbar (1996). The volume of the metering chamber and the expansion chamber are 63.0 and 17.6 mm^3; the diameters of the valve orifice and the actuator nozzle are 0.7 and 0.5 mm, and the discharge coefficients of these are 0.61 and 0.5. These values reflect practical systems in common use.

Initially, it is a saturated vapour and liquid mixture presenting in the metering chamber. When the valve orifice opens, the fluids are released into expansion chamber. With the vapour generated, a two-phase flow is formed. The flow will be initially choked through valve orifice as the pressure difference reaches the sonic conditions. With the loss of mass in the metering chamber, the pressure