Next-Generation Nasal Drug Delivery Exploiting Non-Newtonian Fluids and Smart Thermoresponsive Materials

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Background

Systemic nasal drug delivery (NDD) as an alternative to oral and parenteral routes has been an area of interest due to its potential for delivery of vaccines and biologics such as proteins and peptides (1). However, there is a lack of literature studying the shear degradation of biologics during atomisation in nasal sprays. This is further complicated as the shear stress generated in unit dose nasal spray devices is not fully understood.

The aim of this study was to design a working computational fluid dynamics model to study the fluid flow and strain rates of simple Newtonian and non-Newtonian formulations in the NasaDose device, Bespak's proprietary unit dose nasal spray. This will be followed up by studying the shear rates in more complex formulations of interest.

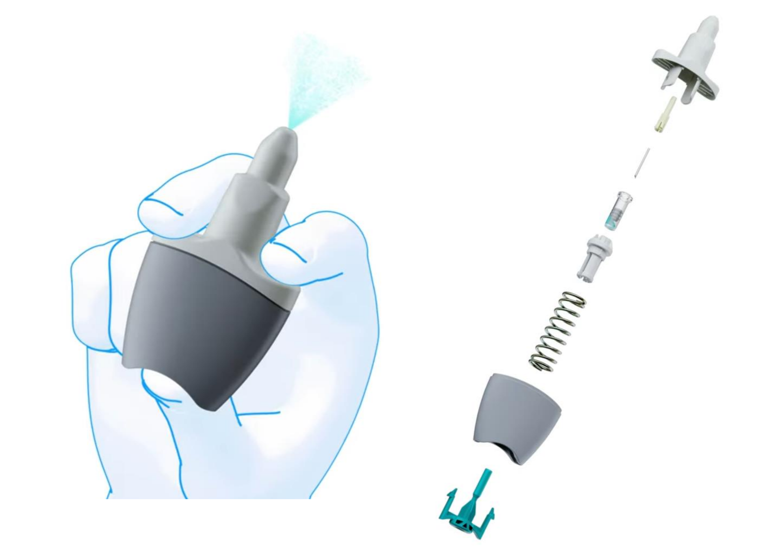

Fig.1. illustrates the Bespak NasaDose device (2)

Methodology

A computer-aided design (CAD) representing the internal geometry of the drug pathway in the NasaDose device was created (Fig.1)

Fig.2. Illustrates the CAD used in this CFD study

Next, the mesh was designed, a total of 4 mesh models were used in this study, [1] surface remesher, [2] automatic surface repair [3] Trimmed (hexahedral) volume mesher, [4] Prism layer mesher (Fig.3)

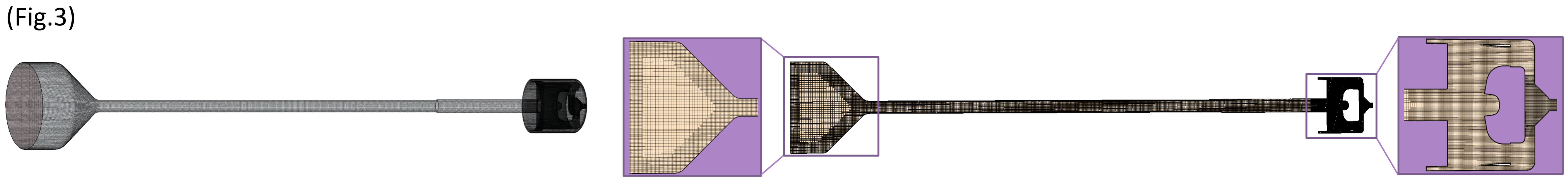

Fig.3. Illustrates the mesh operation used in this CFD study

The next step was setting up the physical models:

1. volume of fluid (VoF), a Eulerian multiphase model, was used as the main physical model (3).
2. Power-law viscosity model was implemented for non-Newtonian fluids.
3. Implicit unsteady flow model was used (4,5).
4. Convective and free-surface Courant-Friedrichs-Lewy (CFL) adaptive time step were also used (6).

Currently, the formulations tested include two Newtonian fluids, water and viscosity standard, 20cP silicone oil. Some aspects of this study were validated using experimental data from Proveris SprayVIEW and Malvern Spraytec.

Results & Discussion

Fluid flow

Here we look at the flow of a **Low-viscosity Newtonian** (water) and **High-viscosity Newtonian** (20 cP silicone oil) formulations in order of increasing solution time in the NasaDose device:

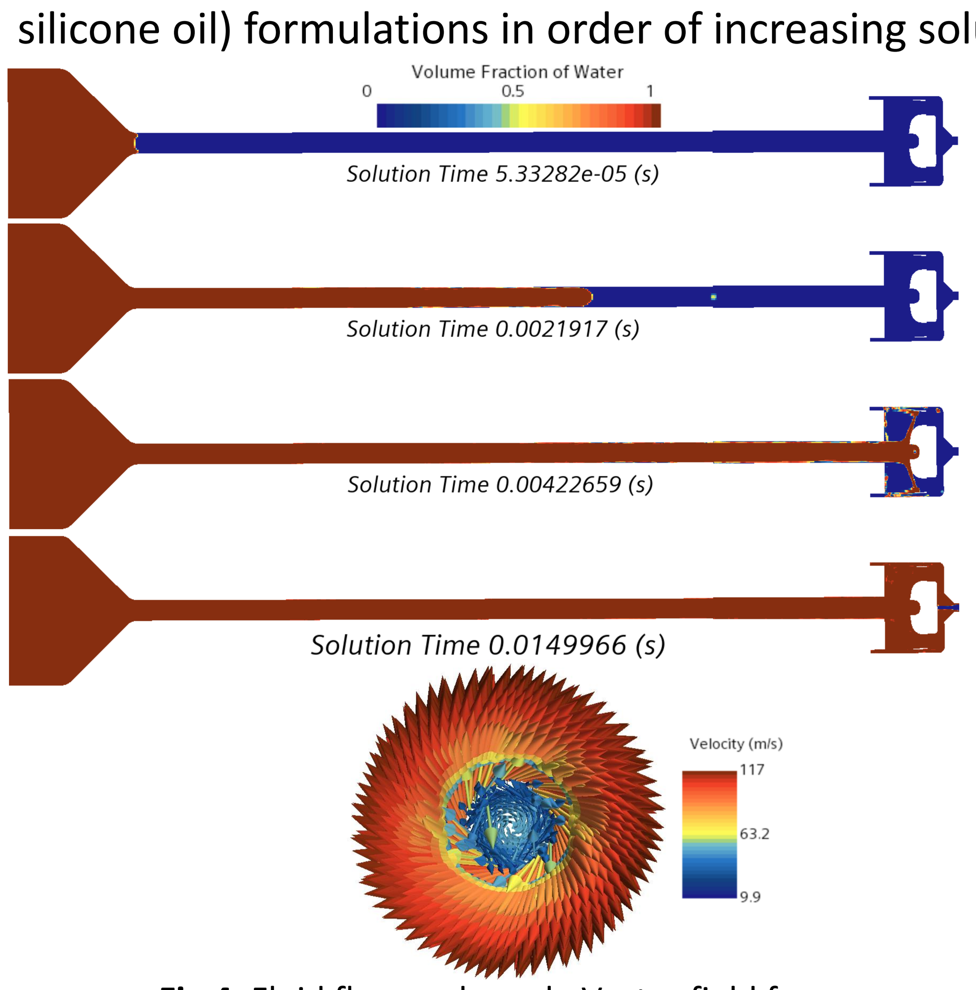

Fig.4. Fluid flow and nozzle Vector field for low-viscosity – water

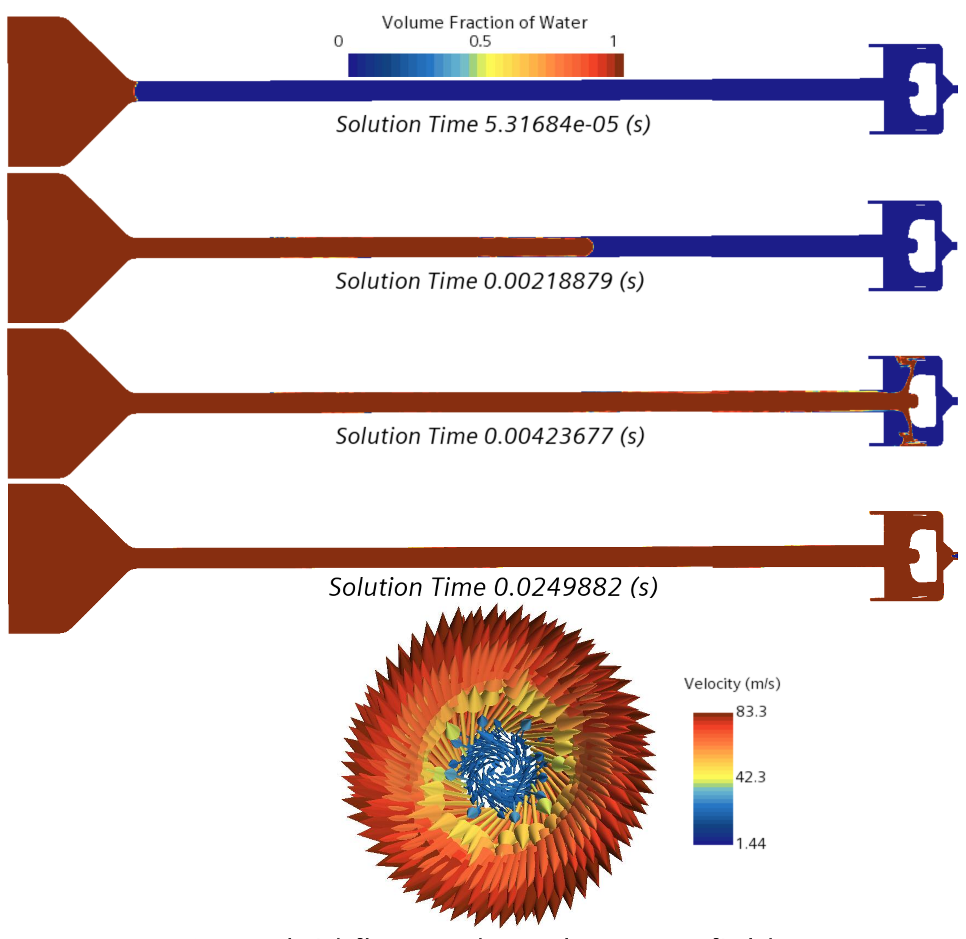

Fig.5. Fluid flow and nozzle Vector fields for high-viscosity – 20 cP silicone oil

As observed in Fig.4 and Fig.5, for low and high-viscosity formulations, it takes approx. 15 and 25 ms for the flow to fully develop at the spray nozzle. This is in line with high-speed video footage from Proveris SprayVIEW where it takes 10-30 ms from actuation to spray observation.

Fluid velocity

Here we will look at the velocity of **Low-viscosity Newtonian** (water) and **High-viscosity Newtonian** (20 cP silicone oil) formulations in the NasaDose device:

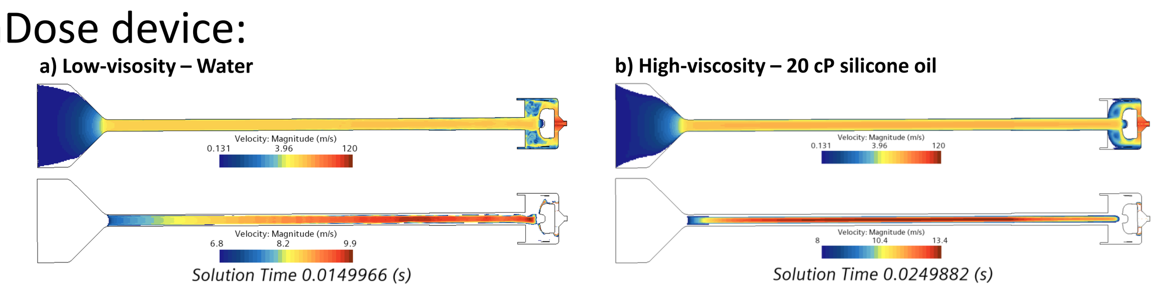

Fig.6. Velocity of formulations during atomisation

As observed in Fig.6, at the spray nozzle, the low-viscosity formulation reaches higher velocities. Additionally, the velocity near the wall is much lower with the high-viscosity formulation due to viscous drag.

However, surprisingly, the velocity of the high-viscosity formulation is slightly higher at the centre of the needle. This may be due to the fact that the Reynolds number at the needle for low-viscosity formulation is 3500, suggesting a transitional flow state while a laminar flow model was used in this simulation.

Additionally, considering the volume of the nasal spray model geometry is 18 µL, we can estimate that the average volumetric flow rate in the device is 18 µL/0.01s (or 1.8x10-6 m3/s). Thus, the average velocity would be 5 m/s which is in line with the velocity data observed in Fig.6.

Strain rate

Here we look at the strain rate of **Low-viscosity Newtonian** (water) and **High-viscosity** Newtonian (20 cPsilicone oil) formulations in the NasaDose device:

Finally, Fig.7 and Fig.8 illustrate that, formulations with higher viscosity will generally have a lower strain rate, this is specially visible at the nozzle spray. However, the exception to thisis at the centre of the needle where the strain rate was higher for the high-viscosity liquid.

In conclusion, VoF proves to be an effective tool for understanding the strain rate in a nasal spray device. However, the high velocity and shear rate of the high-viscosity formulation should be further explored as this is unexpected. Additionally, further research on implementing shear thinning formulation to these simulations is required.

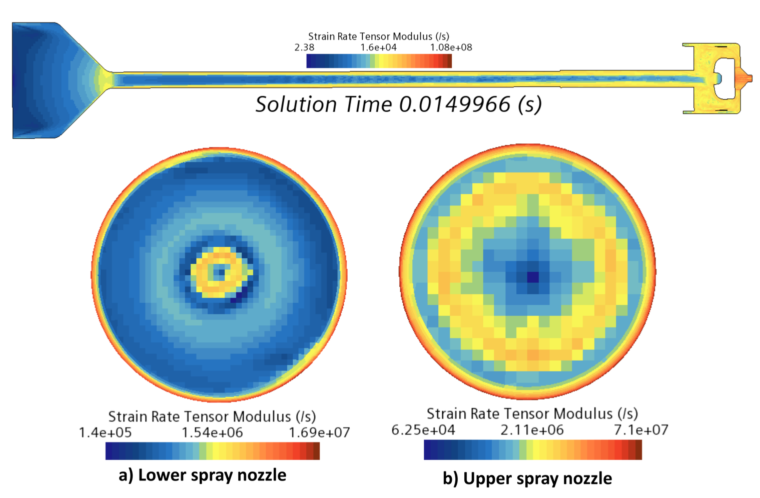

Fig.7. Strain rate of low-viscosity – water during atomisation

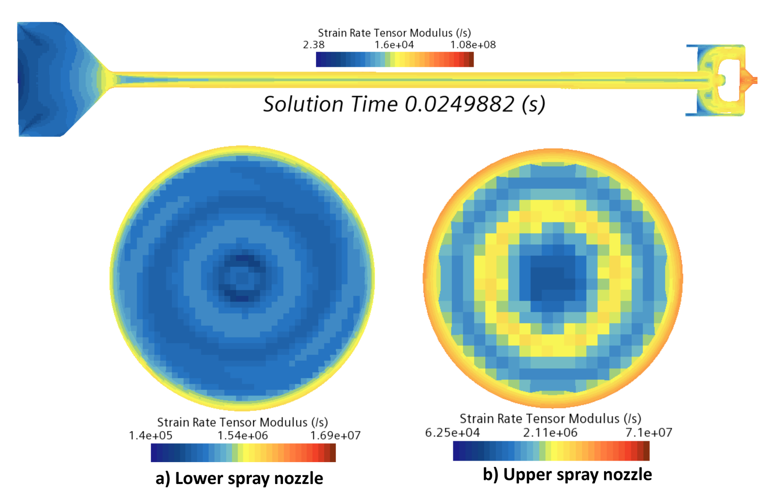

Fig.8. Strain rate of high-viscosity – 20 cP silicone oil during atomisation

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