Effects of viscosity, pump mechanism and nozzle geometry on nasal spray droplet size

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Abstract

In this work the atomization behavior of a nasal spray system has been investigated by laser diffraction. The effects of formulation viscosity, pump mechanism and nozzle geometry on the droplet size produced by a nasal spray were investigated. The droplets size was also investigated as a function of actuation conditions as this is a critical factor in determining potential patient use.

Introduction

Droplet size is a critical factor in the performance of a nasal spray as it affects the location of deposition within the nasal cavity and hence the bioavailability and bioequivalence of the drug [1]. Producing the appropriate droplet size independently of the actuation conditions is critical to ensuring that the delivered dose is independent of operator. The factors affecting actuation independent operation are a combination of formulation rheology, pump mechanism and nozzle geometry. Nasal spray formulations require a delicate balance between increasing viscosity to improve stability and retention on the nasal mucosa and reducing viscosity to provide good atomization behavior [2, 3]. In this work, formulations with different viscosities have been tested using different pump mechanisms and nozzle geometries in order to assess the dependence of the droplet size on actuation conditions for these systems.

Materials and Methods

Atomization dynamics were assessed through droplet size measurements carried out by laser diffraction (using a Malvern Spraytec). Data was recorded at a rate of 2.5 kHz, producing a particle size distribution every 400 microseconds, enabling the formation, stable and dissipation phases to be characterized in detail. An average particle size was obtained for each test from the stable phases of the three actuations [1]. The nasal sprays were actuated automatically using a velocity controlled actuator (Proveris Scientific), using actuation profiles with velocities of 40, 70 and 100mm/s, at a distance of 30mm from the laser beam.

Measurements were carried out using two commercially available pumps, Equadel and VP7 (Valois). The actuation mechanism for each pump is designed to minimize the effect of actuation conditions. The pumps were used in combination with three nozzles with small, medium and large orifice diameters. These systems were tested with three model formulations with different concentration of polyvinylpyrrolidone (PVP), 0%, 0.5% and 1% in water. The PVP increases the Newtonian viscosity of the liquid, whilst elasticity is relatively unaffected, enabling the effect of viscosity on droplet size to be investigated.

Results and Discussion

Figure 1 shows the median particle size for the Equadel and VP7 pumps as a function of increasing viscosity (%PVP), using actuation velocities of 40, 70 and 100mm/s. For both pumps the droplet size increases with %PVP and shows only limited variation in particle size with actuation velocity for lower viscosities (water and 0.5% PVP). However, the 1% PVP solution shows a decrease in droplet size with increasing actuation velocity. This demonstrates that at lower viscosities complete atomization has been achieved under all actuation profiles, where as the higher viscosity 1% PVP solution is not completely atomized at low actuation velocities.

Figure 2 shows the median size as a function of time for each formulation and pump, actuated at 70mm/s. These profiles show that as well as the increase in particle size, there is a decrease in the duration of the stable phase as the viscosity increases. For water, the profile of the VP7 pump shows a stable phase of over 300s, which decreased slightly to 250s for 0.5% PVP. However the 1% PVP sample shows a much shorter stable phase and this is only achieved at the end of the profile. The effect is less pronounced for the Equadel pump where there is little difference in the size and duration of the stable phase between the water and 0.5%PVP samples. However, at 1% PVP a larger more variable particle size is observed for a much shorter duration indicating incomplete atomization of this formulation under these actuation conditions.

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Finally the effect of the nozzle orifice diameter on particle size was investigated using the Equadel pump. Figure 3 shows the size profiles for the small and large orifice diameter nozzles as a function of viscosity (%PVP), actuated at 70mm/s. This shows that a similar increase in droplet size with viscosity is observed for both nozzles; however there is a significant difference in the length of the stable phase. As the stable phase is much longer for the small orifice diameter nozzle, more of the dose from this nozzle can be delivered as small droplets.

Figure 4 shows the actuation velocity dependence of the all three nozzles using the 0.5% PVP formulation. This shows that the droplet size is independent of actuation velocity for the small and medium orifice diameter nozzles, with the medium orifice diameter nozzle producing a smaller droplet size. At high actuation velocities the large orifice diameter nozzle produces a similar droplet size to the medium nozzle, however the droplet size is significantly larger for this nozzle at lower actuation velocities. Finally, the duration of the stable phase decreases as the nozzle orifice diameter increases, as such a much lower volume of small droplets will be delivered by the large orifice diameter nozzle. Hence, the medium orifice diameter will provide the optimum conditions for a nasal spray with a smaller droplet size produced under all actuation conditions.

References

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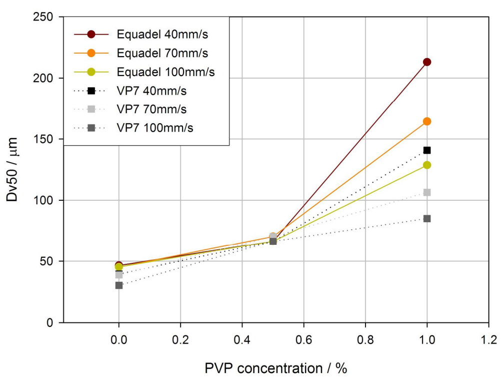

Figure 1. Dv50 vs PVP concentration for Equadel and VP7 pump

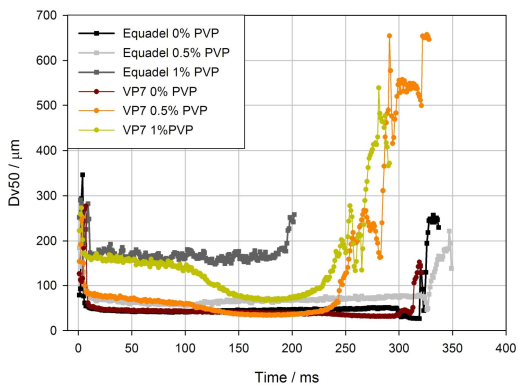

Figure 2. Size histories for Equadel and VP7 for 0%, 0.5% and 1% PVP

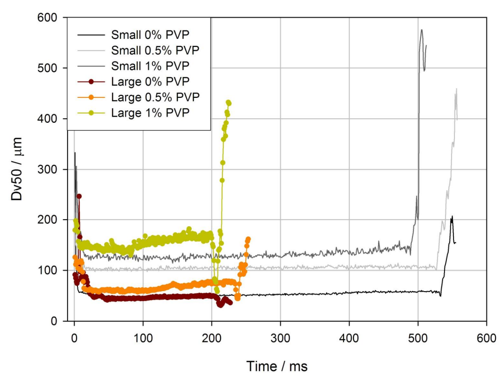

Figure 3: Size histories for Equadel pump with small and large nozzles vs PVP concentration at 70mm/s

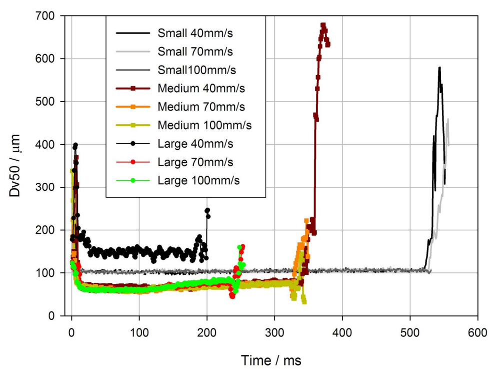

Figure 4. Size histories for Equadel pump, 0.5% PVP with small, medium and large nozzles vs actuation velocity