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Deagglomeration of dry powder pharmaceutical aerosols

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Abstract

The effect of turbulence and mechanical impaction on dry powder aerosol deaggregation was tested using a novel powder deagglomeration rig, with fine particle fraction ($FPF_{ED<5.6\ \mu m}$), defined here as particles sized smaller than 5.6 μm, measured using an Anderson inertial impactor. Powder from GlaxoSmithKline Ventodisks™ was deaggregated either using turbulence generated with a ring of impinging jets, or by impacting the powder on bars of a wire mesh. This deaggregation was compared with deaggregation achieved with the GlaxoSmithKline Diskhaler. The turbulence levels in the test rig and at the exit of the Diskhaler were quantified using laser Doppler velocimetry (LDV). In addition, the Ventodisk powder's auto-adhesion properties were altered by introducing the powder into a high humidity environment (25 °C and 25% R.H.) and then deagglomerated by both the rig (using turbulence as the primary deagglomeration mechanism) and the Diskhaler. Fine particle fractions were found to increase from 13 to 24% as the level of turbulence in the rig was increased. However, fine particle fractions found with the Diskhaler were 35%. Turbulence levels found in the rig at the highest jet flow rate were significantly higher than that at the outlet of the Diskhaler, leading to the conclusion that turbulence is not the only method of deaggregation in this inhaler. The humidified powders were significantly more difficult to deaggregate, giving a $FPF_{ED<5.6\ \mu m}$ of 9% when using the rig and 15% when using the Diskhaler. Fine particle fractions produced when deagglomerating the powder with the wire meshes were similar to those produced without a mesh, showing that mechanical impaction had little effect. The results underline the utility of having a rig that can explore the ability of a powder to deagglomerate with controlled variations in the deaggregation forces.

Keywords: Aerosol; Dry powder inhaler; Diskhaler; Turbulence; Anderson impactor; Powder deaggregation; Powder deagglomeration; Powder inhalation

1. Introduction

Dry powder inhalers are used to deliver drugs to the lungs for treatment of pulmonary and systemic diseases. Such inhalers entrain a small amount of fine drug powder into an inspiratory air stream. If the particles are of an appropriate aerodynamic diameter, they will enter the lungs and, if deposited in the deepest reaches of the lungs, this may lead to uptake into the bloodstream.

To be effective, an inhaler must protect the powder from the ambient environment, dose a

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repeatable amount each time activated, and deagglomerate the powder into particles of a respirable size. In addition, an inhaler should be portable and easy to use. Of these issues, powder deagglomeration is one of the most problematic (Craig et al., 1998).

Powders of a size small enough to be inhaled into the lung tend to agglomerate since the interparticulate forces are large compared with aerodynamic and gravitational forces (Craig et al., 1998; Finlay, 2001; John et al., 1996). Due to this, an inhaler must generate forces that will not only entrain the powder, but also deagglomerate it for inhalation. Entrainment of these fine drug particles in an inhaler is aided by the addition of much larger carrier particles (e.g. lactose). The larger carrier particles are more susceptible to aerodynamic forces during entrainment, allowing for a more efficient uptake. This allows the drug particles to be more readily entrained, but there is still the problem of deagglomeration of the drug particles from the carrier particles. Of particular interest is defining which forces generated by an inhaler are the most effective at deagglomerating the powder.

At present, the principal forces leading to powder deagglomeration in inhalers remain unclear. Certain literature points to turbulence being a principal source of deaggregation, (Craig et al., 1998; Donna et al., 1996; Wen-I. Li et al., 1996) but deagglomeration forces caused by mechanical impaction, particle uptake, and mechanical vibration may also be important (Craig et al., 1998; Finlay, 2001). In actual inhalers, some combination of these forces may be responsible for powder deagglomeration. However, two of the main forces that may cause deagglomeration are:

- Aerodynamic lift and drag perhaps generated by turbulence as eddies sweep by particles or during particle entrainment by shear.
- Sudden acceleration of a carrier particle causing a separation force. This would occur when the carrier particle impacts on a surface, and suddenly reduces its velocity, or during sudden changes in carrier particle velocity when being passed through a turbulent flow, as well as during mechanical vibration.

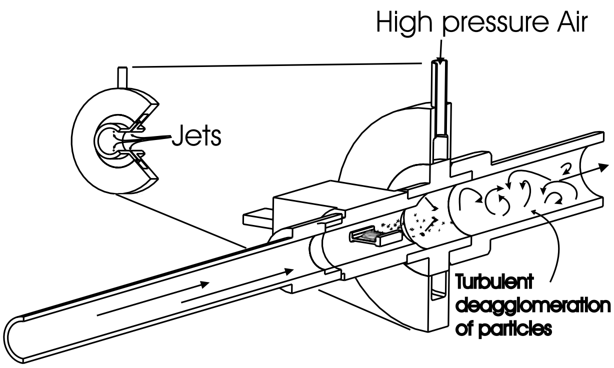

Fig. 1. Schematic of powder being entrained and deagglomerated by turbulence in the rig.

Although the mechanisms in inhalers that are designed to deagglomerate the powder produce a combination of the above forces, it is useful to examine these mechanisms separately to determine the effect each mechanism has on particle deagglomeration.

In this work, the deaggregation mechanisms of turbulence and mechanical impaction are examined separately using a novel powder deagglomeration rig. The effect of deagglomeration by these mechanisms is compared with the deagglomeration from the GlaxoSmithKline Diskhaler.

2. Experimental setup

2.1. Dry powder deagglomeration rig

To test the mechanisms that deagglomerate the dry powder aerosols within an inhaler a deagglomeration rig was designed. The rig entrains a dose of powder into the air stream, and then after entrainment, it exposes the powder to either a controllable level of turbulence (Fig. 1) or a mesh (Fig. 2).

The rig is shown in Fig. 3, The powder is placed on the powder tray, and then weighed using an analytical balance. The powder tray is then inserted into the flow, generated by a 1/3 HP vacuum pump, allowing the powder to be entrained. The entrained powder becomes exposed to turbulence created by the jets, and the effect of

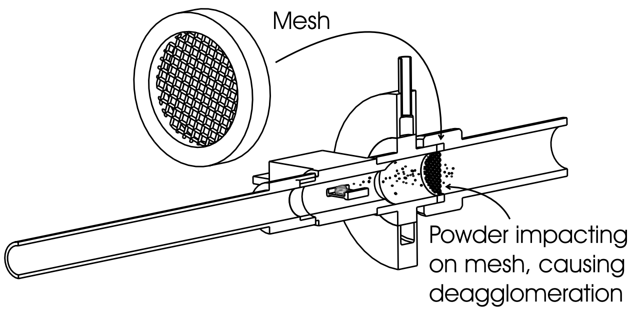

Fig. 2. Schematic of powder being entrained and deagglomerated by impaction on bars of a mesh in the rig.

turbulence on powder deaggregation can be measured. The flow rate through the jets can be adjusted to control the level of turbulence. Alternatively (as shown in Fig. 2) a mesh can be placed in the path of the powder causing the powder to impact on the mesh bars, thus testing the mechanical impaction method of deaggregation. The level of deaggregation achieved is quantified by using a non-viable Anderson mark II inertial cascade impactor (ThermoAnderson, Smyrna, GA).

2.2. Deagglomeration experimental procedure

A schematic of the experimental setup is shown in Fig. 4. From this figure it can be seen that the powder enters the horizontally positioned Anderson impactor with preseparator attached. The horizontal position of the impactor should not alter its particle size selection (Willeke and Baron, 1993). The impactor measures the size distribution of the powder that enters it using inertial impaction. The plates of the impactor have been previously greased with 316 silicon spray grease (Dow Corning, Midland, MI), applied evenly across each plate twice with a 15 min drying period after each application. This is done to eliminate the bounce of the powder particles off of the plates, which can give an incorrect size distribution (Vaughn et al., 1989; Nurtan et al., 1980). The preseparator was not sprayed with silicon grease. Also, the inlet of the Anderson impactor preseparator was modified to allow a smoother entrance, and stage seven was removed to allow for a simpler assay.

The impactor flow rate was set at 60 lpm using a mass flow meter (Matheson Gas Products, 0–100 lpm), This flow rate is higher than the standard flow rate of 28.3 lpm (1 SCFM) normally used in the Anderson impactor but is more representative of human inspiratory flow rates in DPI's. Since particle entrainment depends upon inhalation velocity, the higher flow rate was used. The Mark II Anderson impactor has been recalibrated at 60 l/min (Nichols et al., 1998), and Table 1 shows the cut points for the Anderson impactor when run at 60 l/min. Using this recalibration the size range of the powder impacted on each plate is known.

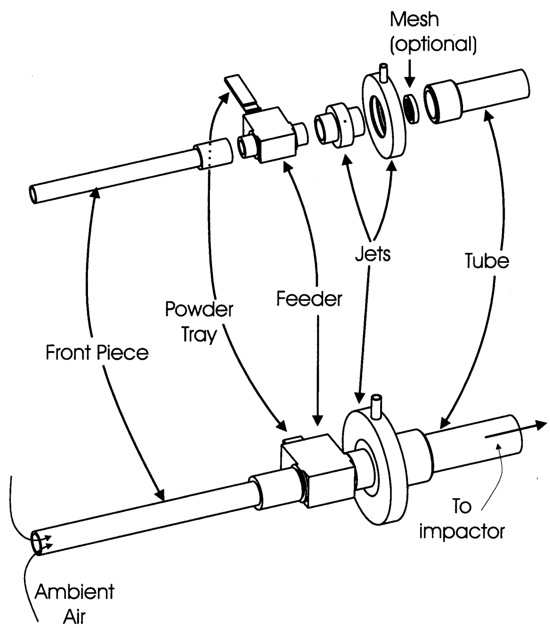

Fig. 3. Schematic of powder deagglomeration apparatus.

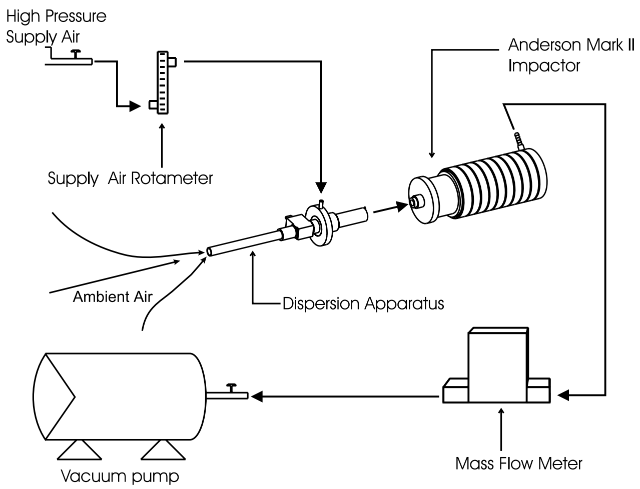

Fig. 4. Schematic of experimental setup.

After dispersion of the powder into the impactor is complete, the apparatus (excluding the front piece), the preseparator, the first impactor sieve, and all the impactor plates are assayed with 3–10 ml of water (the amount depending on the piece). The solution containing the powder from the plate is then analyzed with UV spectroscopy (Hewlett Packard Diode array Spectrophotometer, model 8452A) to determine the concentration of drug present. This determines the amount of drug deposited on each stage. Examining Table 1, any drug measured on stages one to five can be considered as successfully deaggregated from the much larger carrier particles. This result can be combined with the amount of powder retrieved from all the portions of the apparatus, not including the powder tray, to give a fine particle fraction ($FPF_{ED<5.6\ \mu m}$) of the emitted dose.

When the jets are used for powder deagglomeration, a high pressure source is attached to the inlet of the jets. This air is metered using a 0–60 lpm rotameter (Omega products, model FL-3663C). Three different flow rates were used in these experiments: jet flow rates of 0, 20, 40 lpm. Because the flow rate through the Anderson impactor was a constant 60 lpm, the flow rate upstream of the jets was less by an amount equal to the flow rate of the jets.

Two different meshes (placement shown in Fig. 3) were used in the deagglomeration rig to test impaction deaggregation. The first (mesh 1) had a 54% obstruction coverage (wire diameter = 457.2 μm, gap diameter-1143 μm), while the second (mesh 2) had an 84% obstruction coverage (wire diameter = 190.5 μm, gap diameter = 228.8 μm). The obstruction coverage should be equal to the percentage of powder impacting on the grid, thus exposing this percentage of the powder to mechanical impaction forces (Finlay, 2001).

2.3. Testing the GlaxoSmithKline Diskhaler

In addition to testing the deagglomeration of powders when exposed to turbulence or impaction, the Diskhaler™ (GlaxoSmithKline) was tested in a similar fashion. The Diskhaler was attached to the tube (with the jets, feeder, tray and frontpiece

Table 1
Cut points for Anderson inertial impactor when used at a flow rate of 60 lpm

Plate number	Aerodynamic diameter (μm) cut point
0	5.6
1	4.3
2	3.4
3	2.0
4	1.1
5	0.51

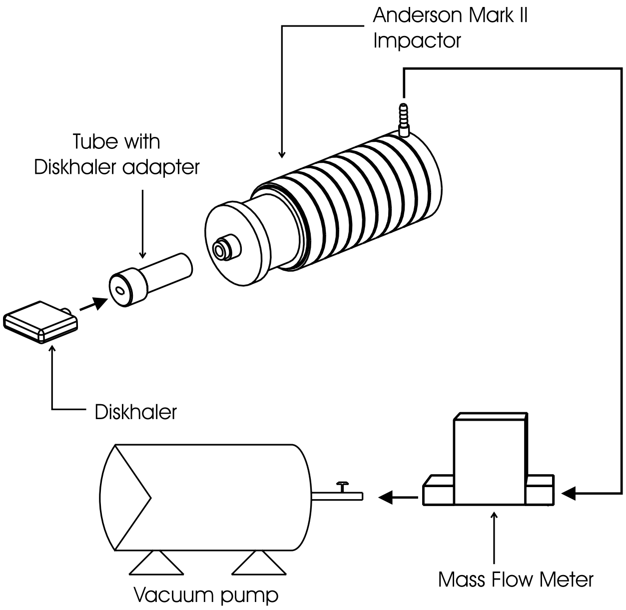

Fig. 5. Schematic of experimental setup with Diskhaler.

removed) with a special adapter that was form fitted to the outlet of the Diskhaler. Otherwise, the experimental setup was the same as that of the deagglomeration rig. A schematic of the deagglomeration tests using the Diskhaler is shown in Fig. 5.

2.4. Laser doppler velocimetry for turbulence measurements

Laser Doppler Velocimetry (LDV) is a method of measuring the velocities of particles passing through the intersecting point of two laser beams. Thus LDV provides a non-intrusive, rapid method of measuring the instantaneous velocity of a fluid at a point, provided the fluid is seeded with particles that follow the flow.

The experimental setup for the velocity measurements is shown in Fig. 6. For the velocity measurements done in this work, a LDV was used (Dantec, He-Ne Laser @ 632.8 nm, Skovlunde, Denmark). A monodisperse aerosol generator (TSI, model 3475, St. Paul, MN) was used to generate a cloud of sufficiently small oil aerosol particles (mean diameter = 2.5 μm) needed for seeding the flow for the LDV. Because the aerosol generator only provides approximately 4 lpm, at the outlet of the aerosol generator, the aerosol rich air is mixed with room air to provide the needed flow rate (60 lpm minus jet flow rate). This diluted aerosol is then passed through the deagglomeration rig and the Dantec LDV is used to determine the velocity of the aerosol downstream of the jets where the tube has been replaced by a pyrex tube to allow the receiving optics to view the light scattered by the passing aerosol particles. A coalescing filter then removes the oil aerosol

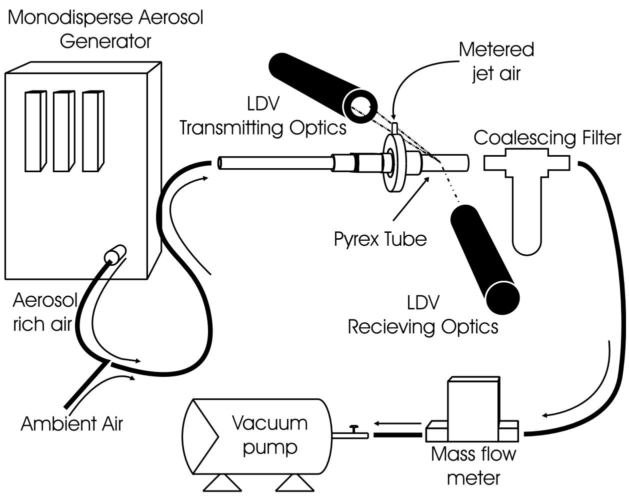

Fig. 6. Schematic of experimental setup for LDV.

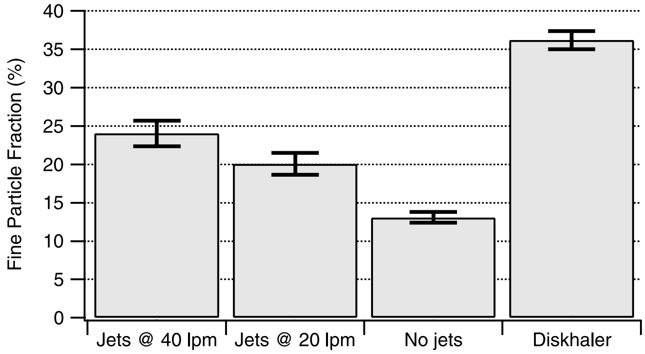

Fig. 7. Fine particle fraction results with varying levels of turbulence from jets. Results from Diskhaler are included. Error bars are standard error.

from the air before it passes through the mass flow meter. The test was repeated for several different locations downstream of the jets.

The velocities downstream of the Diskhaler were measured with a similar method. The deagglomeration rig was replaced with the inhaler which was directly attached to the pyrex tube. The inhaler was enclosed in a sealed container which was supplied with the monodisperse aerosol, so that the inhaler's output is rich in aerosol particles allowing the turbulence generated by the inhaler to be measured with the LDV.

2.5. Test Powders

For the all of the deagglomeration experiments, powder from GlaxoSmithKline Ventodisks (the disk-shaped blister packs used in the Diskhaler) was used. The powder contains carrier lactose (approximate mean diameter 60 μm) and the drug Ventolin (Albuterol Sulfate) (approximate mean diameter 2.5 μm). This powder was chosen for several reasons: it is a well-known pharmaceutical powder, it is easy to remove from the Ventodisks, it is soluble in water (making the assay simpler), Albuterol Sulfate has large, linear UV absorbance over a sizable range, and it is inexpensive. To transfer the powder unto the tray, the Ventodisk is cut open and the powder is emptied into a vibrating spoon. The vibrating spoon is then used to transfer the powder unto the tray, which is weighed on an analytical balance.

To measure the effect of turbulence on powders of differing adhesion properties, the powder from the Ventodisk was exposed to humidity before being dispersed. Humidity generally increases adhesion in lactose powders (Podczeck et al., 1997), and the Ventodisk powder is largely lactose, so that this was a simple way of altering the adhesion properties of the powder. The powders were stored in a humidity closet at 100% R.H. and 25 °C for 15 min. Since the Diskhaler could not be used to test these powders if the powders were removed from the blister packs, the powder was left in the blisters, but a small hole (1 mm diameter) was punched in the foil of each blister. This allowed the transfer of humidity from the ambient in the closet to the powder in the blister pack.

3. Experimental results

3.1. Effect of turbulence on deaggregation

The experiments on turbulent deaggregation used the Ventolin powder from the Ventodisks. The deaggregation was tested with the jet flow rate at 40, 20 and 0 lpm. The amount of drug measured with the assay on all parts of the apparatus compared with the amount of drug weighed gives the recovery for the tests. For all the experiments performed, with the particle deagglomeration apparatus in this study, the recovery was between

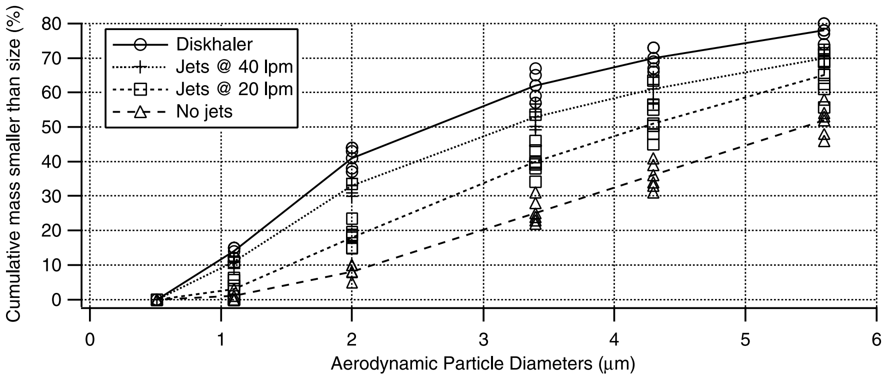

Fig. 8. Cumulative size distribution of turbulence induced deaggregation. Lines show average results.

95 and 110%. This recovery is reasonable, validating this method.

Fig. 7 shows the $FPF_{ED < 5.6\ \mu m}$ of the powder when deaggregated by differing flow rates through the jets. The error bars shown are standard error. Fig. 8 shows the cumulative mass distribution for powder in the respirable range (< 5.6 µm, i.e. anything on plates 1 through 6 in the Anderson impactor, compared with the total amount found in the impactor, not including preseparator).

3.2. *Turbulence measurements using laser doppler velocimetry*

The turbulence measurements were performed on both the Diskhaler and the deagglomeration rig as discussed in Section 2.4. Since turbulence decays downstream from a production point, comparison of the results of the tests some require assumption as to where the turbulence was being generated in the inhaler. As shown in Fig. 9 the hole in the side of the Diskhaler mouthpiece was used as the origin of the turbulence. Thus in Fig. 10, the turbulent velocities are shown measured a distance downstream of either the centerline of the jets (in the rig) or the hole in the mouthpiece (Diskhaler). All measurements are along the centerline of the tube.

3.3. *Effect of mechanical impaction on deaggregation*

To test mechanical impaction, a mesh was placed in the deagglomeration rig between the jets and the tube (as shown in Fig. 3).

The results of the experiments are shown in Fig. 11. Also shown is the amount of drug that was assayed off the mesh following the experiment. This is important because the powder that remains on the grid, even if it was deagglomerated by the grid, will not be included in the $FPF_{ED < 5.6\ \mu m}$ measured by the experiment, as the powder never entered the Anderson impactor.

Fig. 12 shows the cumulative mass distribution for particles in the respirable range.

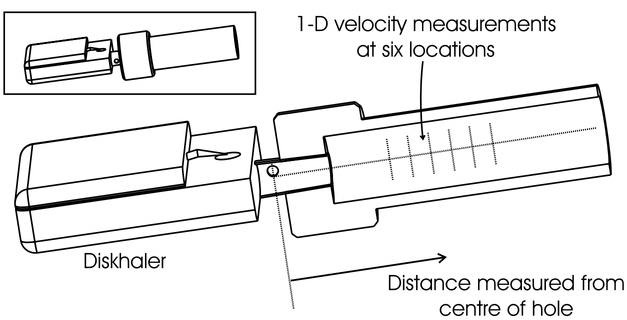

Fig. 9. Measurement location of velocities downstream of Diskhaler with LDV.

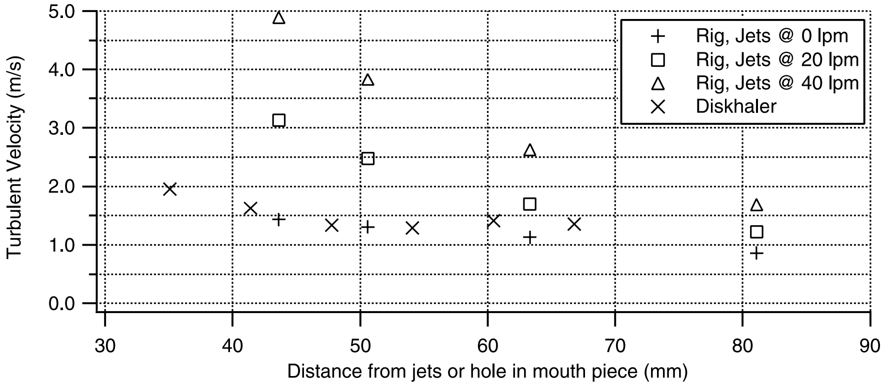

Fig. 10. One dimensional streamwise turbulent root mean square velocities u' along the centerline of the tube

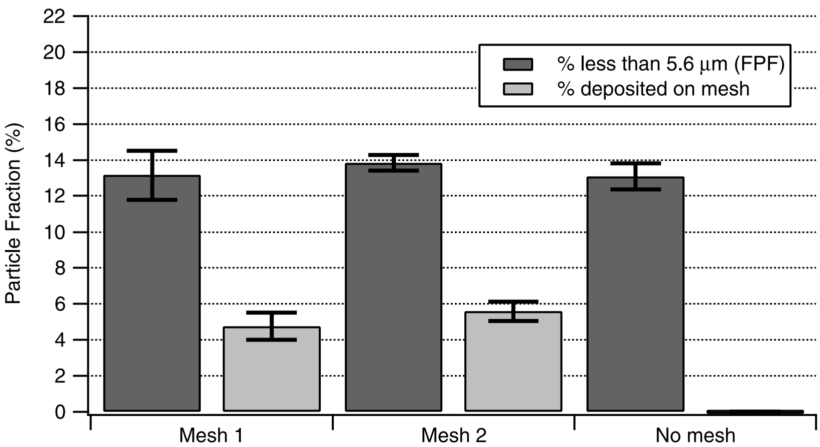

Fig. 11. Deaggregation results of adding meshes for mechanical impaction. Included is the amount of drug deposited on the mesh. Error bars show standard error.

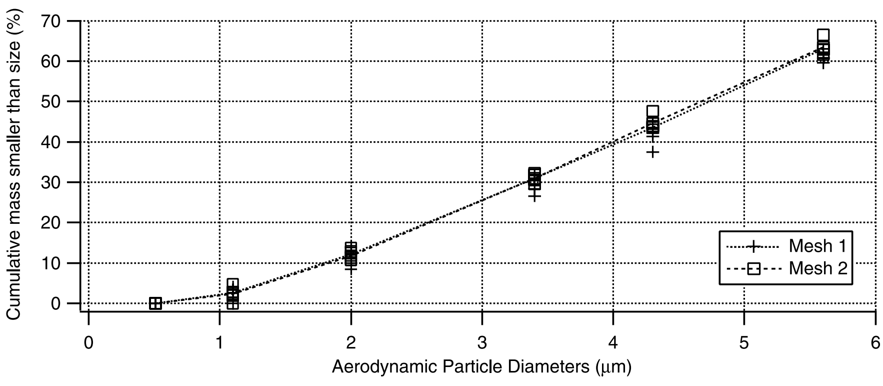

Fig. 12. Cumulative size distribution for mechanical impaction.

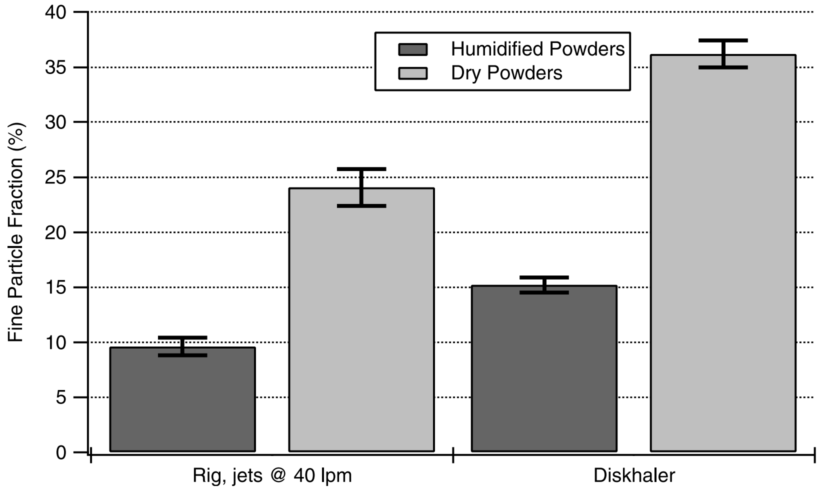

Fig. 13. Fine particle fraction of powders stored @100% R.H. and 25 °C compared with powders stored in dry conditions. Error bars shown are standard error.

3.4. Deagglomeration of humidified ventodisk powder

Fig. 13 shows the results of the humidity exposure study (note that the results from Fig. 7 are repeated to illustrate the effect of storing powders at high humidity by giving a direct comparison between $FPF_{ED<5.6\mu m}$ of the dry and humidified powders). Fig. 14 shows cumulative mass distribution for these tests.

4. Discussion

4.1. Turbulent deaggregation

Figs. 7 and 8 show that there is a definite correlation between the flow rate through the jets and the amount the Ventolin deaggregated from the carrier particles, while Fig. 10 shows that as the jet flow rate is increased the fluctuating velocity increases. Therefore there is a correlation seen between the turbulence velocity and the deaggregation that occurs. Or, to put it another way, as the turbulence increases, the deaggregating force increases. Finlay, (2001) discusses the deaggregat-

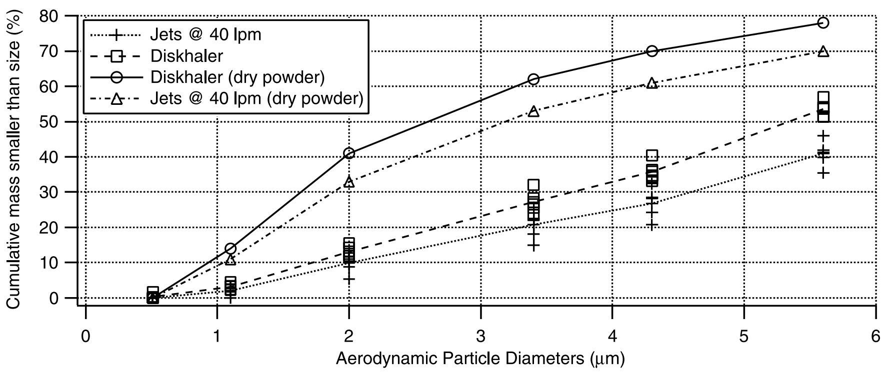

Fig. 14. Cumulative size distribution of powders stored @100% R.H. and 25 °C when deagglomerated with rig and Diskhaler. Average cumulative size distribution for powders stored in dry conditions are also shown.

ing forces that may be involved as a pharmaceutical powder is passed through a turbulent flow field. He concludes that the turbulent deaggregation force increases as the fluctuating velocity increases. This is what is seen here experimentally.

The deagglomeration rig was designed to keep all variables the same while adjusting the flow rate through the jets. However, as the flow rate through the jets increases, the flow rate through the frontpiece and feeder is reduced by an equal amount. This means that the entrainment velocity (the flow rate through the feeder) changes with the changing jet flow rates. If the entrainment velocity has any part in the deagglomeration of the dry powder formulation then it could alter the controlled portion of the test. However, since the entrainment velocity decreases with increasing jet flow, but $FPF_{ED<5.6\ \mu m}$ is observed to increase with increasing jet flow rate, this does not alter our conclusion that increasing the turbulent velocity increases particle deaggregation.

4.2. Mechanical impaction

As is shown in Fig. 11 the meshes do not significantly affect the $FPF_{ED<5.6\ \mu m}$ produced by the deagglomeration rig. In more detail, mesh 1 produced a $FPF_{ED<5.6\ \mu m}$ of 13.2%, mesh 2 produced a $FPF_{ED<5.6\ \mu m}$ of 13.8%, and in the case of no mesh the $FPF_{ED<5.6\ \mu m}$ was 13.1%. The increase in $FPF_{ED<5.6\ \mu m}$ does follow the increase in obstruction coverage, but the increase in $FPF_{ED<5.6\ \mu m}$ is insignificant. In fact, the difference between the effect of mesh 1 and mesh 2 is not statistically significant ($P = 0.67$), neither is the difference in $FPF_{ED<5.6\ \mu m}$ between mesh 1 and no mesh ($P = 0.96$), or mesh 2 and no mesh ($P = 0.465$). Mesh 2 does have more deposition on itself (5.45%), which does make sense in that its obstruction coverage is 84% compared with the 54% of mesh 1 (average deposition of 4.75%). But again, this difference is not significant ($P = 0.35$).

From these results it can be seen that the meshes used did not have any effect on the $FPF_{ED<5.6\ \mu m}$ produced by the deagglomeration rig. If they do aid in the deagglomeration of the drug particles from the carrier particles, it is offset by the amount of drug that remains on the bars of the mesh. To ensure impaction of a particle traveling into a bar of the mesh, the Stokes number (Stk) of the lactose carrier must be > ten (Marple et al., 1993). Using the equation

$$Stk_c = \frac{U \rho_{particle} d_c^2}{18 \mu D}$$

with Stk_c = carrier particle Stokes number, U = velocity of carrier particle = 3.5 m/s, $\rho_{particle}$ = density of carrier particle = 1000 kg/m^3, d_c = diameter of carrier particle = 60μm, μ = viscosity of air = 1.8×10^{-5}kg/m per s, D = Diameter of mesh bars = 457.2 μm (mesh 1) or 228.8 μm (mesh 2) the Stokes numbers then are: Stk_c(mesh 1) = 52, Stk_c(mesh 2) = 245, and are both well over 10. Therefore, the suggestion that 54% of the powder impacts on mesh 1, and 84% of the powder impacts on mesh 2 is reasonable.

From the above results it can be deduced that collision induced deaggregation (of Ventodisk powder) is not effective at velocities of 3.5 m/s or lower. These results are interesting, as screens and meshes are common among dry powder inhalers. Of course, the velocity prior to impaction would be important when applying this result to specific dry powder inhalers. The Diskhaler, for example, contains a mesh just downstream of the uptake region. If the flow rate through the uptake region is 20 lpm (explained below), and the cross-sectional area just upstream of the grid is approximately 1 cm^2, then the velocity prior to impaction is 3.3 m/s, very similar to that tested in the rig. Thus the grid in the Diskhaler probably does little to aid in deaggregation of the dry powder.

4.3. Effectiveness of the deagglomeration rig compared with the Diskhaler

As can be seen in Fig. 7, the Diskhaler gives a much higher $FPF_{ED<5.6\ \mu m}$ when compared with the deagglomeration rig, even at the highest flow rate through the jets. Yet, the turbulence velocity of the flow shown in Fig. 10 is much lower for the Diskhaler than it is for the deagglomeration rig with the flow rate through the jets at 40 l/min. Since it is clear that the turbulence does have an effect on the deaggregation of the powder (as

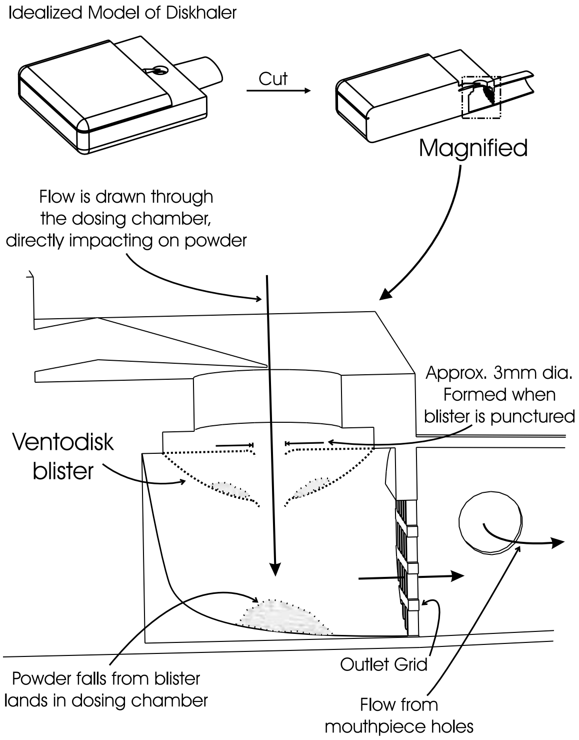

Fig. 15. Close-up sketch of Diskhaler entrainment region. Powder falls from blister when punctured. When a flow is passed through the inhaler (intake of breath, in-vitro with vacuum pump) a jet is formed from the hole punched in blister. Also, flow comes from holes on either side of the mouthpiece.

discussed in Section 4.1), yet the $FPF_{ED<5.6\ \mu m}$ for the Diskhaler is higher than the rig while the turbulence measured is lower, then it can be asserted that the deaggregation from the Diskhaler is not entirely from turbulence. There is the possibility that the powder impacting on the grid in the entrainment region of the Diskhaler is causing the increased deaggregation. However, the data collected from powder impacting on the meshes in the deagglomeration rig does not support the theory that mechanical impaction plays this large a role in the deagglomeration of the Ventodisk powder.

Another explanation is that the relative velocities between the powder and entrainment air is large in the uptake region of the Diskhaler. Fig. 15 is a sketch of the entrainment region of the Diskhaler. When the Ventodisk blister is punctured, the powder falls into the inhaler's uptake region. When air is passed through the inhaler it comes from two main areas: the holes on the sides of the mouthpiece, and through the hole in Ventodisk blister. A jet is formed as the air passes through the hole in the blister. The velocity of this jet is unknown, but it can be estimated by making the assumption that the resistance through the holes in the blister pack is similar to the resistance through the holes on either side of the mouthpiece. If so, 1/3 of the air passes through the blister pack and the rest flows through the holes in the mouth piece. In this case then, of the flow rate of 60 lpm, 20 lpm impinges directly on the powder in the uptake region of the inhaler. If the hole in the Ventodisk blister is 3 mm, this corresponds to a jet velocity of 47 m/s. In contrast, in the entrainment region of the deagglomeration rig the average velocity is 2.6 m/s (flow rate through entrainment region is 20 l/min when the jets are at 40 l/min and the diameter of the entrainment region is 12.7 mm).

This is a drastic difference in entrainment velocities, which may account for the discrepancy in $FPF_{ED<5.6\ \mu m}$ between the rig and inhaler. Also, the geometry of the two uptake regions are quite different. Fig. 16 shows that the rig entrainment region is a flat plate in a cross flow, and the uptake of the carrier particles probably occurs by a shear layer lift or drag force forcing the powder off the tray and entraining it in the flow (Finlay, 2001). In the Diskhaler, however, the jet through the blister pack impinges at a 90° angle to the surface the powder is laying on. This may cause the carrier particles not to follow the flow quite as readily, exposing the drug particles on the surface

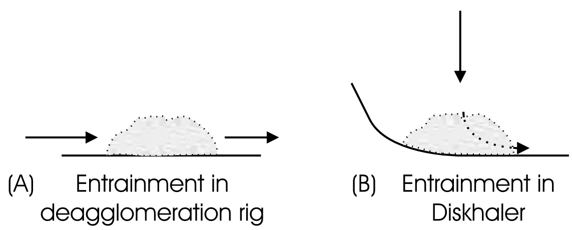

Fig. 16. Uptake in (A) the deagglomeration rig, and in (B) the Diskhaler. In the rig, the surface the powder is entrained from (the powder tray) is parallel to the flow, in the Diskhaler the entraining air flow is at about a 90° angle to the surface the powder is laying on.

to a greater drag force. This theory proposes that the physics behind the removal of drug particles from the carrier particles is the same for turbulent induced deaggregation as it is for uptake deaggregation, only that the relative velocity between the carrier particle and a nearby air flow is greater during uptake.

Turbulence is generally thought to have a large effect on the deaggregation of dry powder pharmaceuticals in dry powder inhalers(Craig et al., 1998; Donna et al., 1996; Wen-I. Li et al., 1996), but the experiments done for this work show that although turbulence does play a role, it is not the only, and possibly not the most important, method of deaggregation. This is interesting because it is possible that turbulence contributes to mouth/throat deposition. Perhaps the turbulence in DPI's should be reduced rather than increased and other methods of powder deaggregation should be examined, such as modifying the uptake region to increase entrainment velocity.

Increasing the efficiency of the rig is a very interesting problem that, due to time constraints, was never properly addressed. If there is significant deaggregation of the powder during entrainment uptake, perhaps the feeder and powder tray should be redesigned to increase the velocity of the entrainment fluid. Care should be taken to keep the rig in such a configuration so that the deagglomerating forces can be isolated, making this a difficult task.

4.4. Using the rig to test humidified Ventodisk powder

The results shown in Fig. 13 illustrate that if the Ventodisk powder is stored in improper conditions, the ability of the deagglomeration rig and the Diskhaler to deaggregate the powder is severely hampered. An important aspect of this is that the $FPF_{ED<5.6\ \mu m}$ from rig and Diskhaler correlate. If only the deagglomeration rig was used to disperse the humidified powder, the results would show that the powder is not suitable for inhalation, which is what dispersion with the Diskhaler has shown. This provides validation for using the deagglomeration rig as a method of testing powders without using a particular inhaler.

5. Conclusion

In conclusion, the powder deagglomeration rig designed was successful at providing useful information about the deaggregating forces that occur in dry powder inhalers. Mechanical impaction, as analyzed, was not an effective deagglomeration mechanism, whereas turbulence was found to have a definite effect on the deaggregation of dry powder aerosols. However turbulence, may not be the only or most effective deaggregation mechanism in dry powder inhalers.

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