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## Evolution of droplet size distribution in selected nebulizers

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**Abstract:** Nebulizers are the class of atomizing devices used to disperse liquids to fine droplets. They found their application in selected technological (typically: small-scale) processes, but their most common use is related to the generation of medicinal aerosols for inhalation. In this work we present the experimental data on the evolution of the size distributions of water droplets generated by two nebulizers (pneumatic and vibrating-mesh) as a result of aerosol mixing with the ambient air. Such a process reflects the real situation, where aerosol emitted from a nebulizer is diluted by additional air sucked by a patient during inhalation. Droplet size distribution was determined by laser diffraction, and these results were further discussed including the data of the aerosol velocity measured by the Laser Doppler Anemometry (LDA). It was demonstrated – as expected - that dilution with the ambient air with moderate humidity results in the intense evaporation of the smallest droplets. However, larger droplet may be saved to a different degree depending on the velocity and geometry of the aerosol cloud emitted from the nebulizer, and on the volume of the diluting air. These parameters have an influence on the droplet coalescence which is another process shaping the droplet size distribution in the studied conditions. The results can deepen the understanding of the mist dynamics which can be applied in various fields of colloidal science and technology.

**Keywords:** spraying, liquid atomization, aerosol dynamics, particle size distribution

### 1. Introduction

Atomization of liquids (spraying) is an important process in many technologies that require dispersions of liquid droplets in the gas phase (typically: air). The obvious advantage of this liquid aerosol, often called a mist, is a very large liquid/gas interfacial surface area, and simultaneously, the minimized mass transfer resistance in the continuous gas phase because of mixing by moving droplets. Therefore, such a contact it is preferentially used during air humidification and in the absorption of gaseous components that are easily soluble in the solvent, i.e. in the cases when mixing and mass transfer in the gas phase needs intensification as a limiting stage of the whole process (Lefebvre and McDonell, 2017). This kind of two-phase system it is opposite to bubbling, where gas is dispersed in the liquid, that allows mixing and the reduction of mass transfer resistance in the liquid phase.

Important large-scale applications of spraying include air cleaning from dust particles (Wang et al., 2004) and fire suppression by water mist extinguishing systems (Grant et al., 2000). Liquid atomization is a common process in the manufacturing of powder products by spray drying, e.g. in the food technology (Woo and Bhandari, 2013; Finnley et al., 2002), pharmaceutical industry (Kramek-Romanowska et al., 2011; Gradoń and Sosnowski, 2014) and cosmetotextiles production (Muñoz et al., 2017). Spraying also allows to obtain a more homogeneous distribution of liquid on solid surfaces, e.g. to cover these surfaces with functional (e.g. protective, colouring, etc.) layers (Chandra and Fauchais, 2009; Hassani-Gangaraj et al., 2015; Heo et al., 2019). It is also met in mineral processing for the uniform application of the liquid during oil agglomeration (Drzymała, 2007). Spraying is preferentially used in the agriculture to apply pesticides and herbicides (Devi et al. 2020). In a common life, the atomization process is often utilized in cosmetics and household products (Lefebvre and McDonell, 2017). Last but

not least, fine droplets produced by liquid dispersion are used as drug carriers delivered by inhalation (Le Brun et al., 2000; Marianecchi et al., 2011; Ochowiak et al., 2019), topical application on skin (Rothe et al., 2011) or on the nasal mucosa (Sosnowski et al., 2020).

In any application there are different requirements regarding the essential properties of the aerosol cloud, i.e. spray geometry, mass output of the atomizing device and size distribution of emerging droplets. These properties can be controlled by the proper selection of atomization principle, the design of spraying nozzle (or of the whole spraying device), and the physicochemical properties of the liquid - mainly: surface tension and rheological characteristics. There is a large amount of data on this subject in the literature (McCallion et al., 1995; Steckel and Eskandar, 2003; Ghazanfari et al., 2006, Beck-Broichsitter et al., 2014, Broniarz-Press et al. 2015; Beck-Broichsitter et al., 2017) so it will be not discussed in details here.

In this paper we focus on a special group of atomizing devices, known as nebulizers. They are typically used to generate aerosols for drug delivery by inhalation, hence they must fulfill the unique requirements comparing to other atomization systems. The droplets must be in the range of 0.1-10  $\mu\text{m}$  to be inhalable, and preferably smaller than 5  $\mu\text{m}$  to reach the lower airways (small bronchi, bronchioles and pulmonary alveoli) (Carvalho et al., 2011; Pirożyński and Sosnowski, 2016). These devices should be compact (preferably: hand-held), and provide the appropriate output rate and spray velocity for an easy and effective use by patients of various age and health conditions (i.e. the breathing profile). Consequently, nebulizers have different designs than other devices used in spray technology, and the detailed knowledge on their operation under various conditions of use is still inadequate. One of the overlooked effects is related to the dynamic evolution of the aerosol cloud which - upon mixing with inhaled ambient air - may result in the essential change in droplet size distribution (DSD). This is a very important effect regarding the optimization of the dose of inhaled drugs delivered to different parts of the respiratory system. Especially now, in the era of COVID-19 pandemic, the quality of medical aerosol delivered to the patients becomes critical regarding both their therapeutic action and a possible transmission of the disease by the exhaled aerosol (Amirav and Newhouse, 2020; Ari, 2020).

Nebulizers are also broadly employed as convenient and reliable atomizers in the various studies in the aerosol science and analytics (Sheehan et al., 2009; Geersten et al., 2012; Grimm, 2020; TSE Systems, 2020), including testing the facemasks that are used for protection against inhaled aerosols (Bałazy et al., 2006). This is why it seems important to look closer at the characteristics of these spraying devices in a more general sense.

## 2. Materials and methods

### 2.1. Nebulizers and droplet size distribution determination

Two types of nebulizers were used in the studies:

- a) Intec Twister Mesh NE-105 (Intec Medical, Cracow, Poland),
- b) Pari Boy SX (Pari GmbH, Germany).

NE-105 nebulizer (Fig. 1a) is a vibrating mesh device (VM) in which the aerosol is formed due to extrusion of multiple liquid streams and shearing them on the surface of the oscillating (100 kHz) polymer membrane with calibrated orifices (Pritchard et al., 2018). This principle of operation allows to generate aerosol of droplets with the predominant diameter within the respirable range, and with the atomization rate up to 0.25  $\text{cm}^3/\text{min}$  (Intec Medical, 2015). This nebulizer is battery operated.

Pari Boy SX nebulizer (Fig 1b) is a pneumatic device (PN) in which the liquid is sucked and disintegrated in the two-fluid nozzle by pressurized air (1.6 bar) delivered from the compressor (Pari, 2011). In this device the aerosol that leaves the nozzle, impacts on the baffles inside the nebulizing chamber, allowing large droplets to separate and drain, while inhalable droplets are emitted outside through the mouthpiece. According to the manufacturer data, liquid atomization rate in this device equals 0.6  $\text{cm}^3/\text{min}$ . The air compressor is supplied from the electric socket.

Both nebulizers were used in the arrangement that allowed to evaluate how mixing of ambient air with the emitted aerosol influences the size of droplets in the cloud, Fig. 2. DSD of aerosol generated by each device was determined by Spraytec diffraction aerosol spectrometer (Malvern Instruments, UK), shown as element no. 3 in Fig. 2. The aerosol was drawn to the measuring zone of the spectrometer 5

by air pump 7 with the rate controlled by valve 6 according to the indications of the anemometric airflow meter (TSI Inc, USA – not shown). In this arrangement, the additional ambient airstream 2 could be mixed with the emitted cloud prior to the droplet size analysis in the spectrometer. The mixed aerosol was introduced to the measuring zone 5 via the bent tube 3 called the USP inlet according to the recommendations for inhalation aerosols (European Pharmacopeia, 2017).

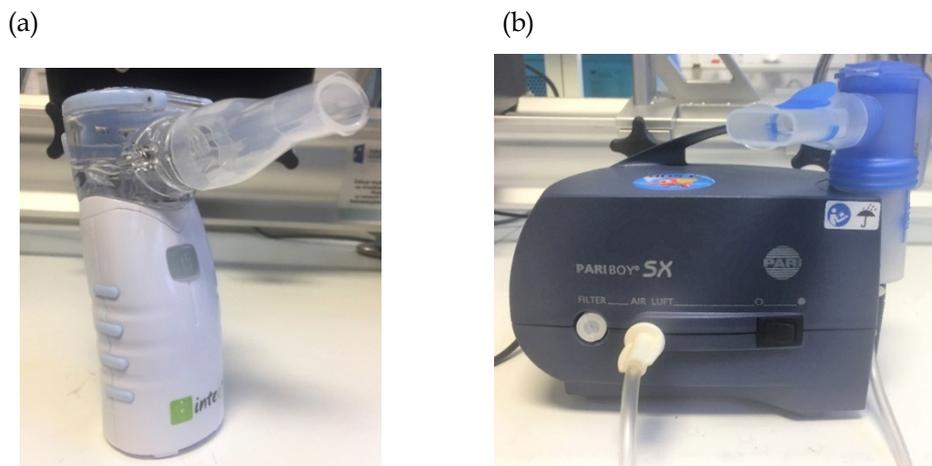


Fig. 1. a - Intec Twister Mesh NE-105 nebulizer: VM; b - Pari Boy SX nebulizer with compressor: PN

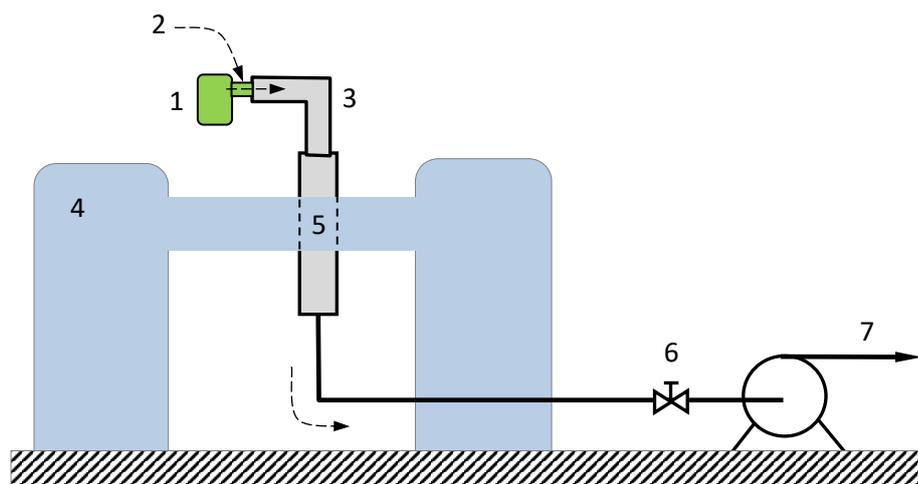


Fig. 2. The schematic of experimental set-up: 1 - nebulizer, 2 - external airflow, 3 - USP inlet, 4 - Spraytec aerosol spectrometer, 5 - measuring zone, 6 - control valve, 7 - air pump

The nebulizers were studied at three configurations: without external flow (i.e. the raw aerosol produced by the nebulizers) and with two values of additional airflow: 6 and 25 dm<sup>3</sup>/min. The case without external flow is not only hypothetical – such conditions may be met in reality when the inhalation flow of a patient is lower than the flow produced generated by the nebulizer. Two other cases imitate air intake during the normal and forced inhalation and correspond to a more typical situation when the inhalation flow exceeds the inhaler output, and must be supplemented by the air from the surrounding environment.

All measurements were done at room temperature (23 ± 2 °C) at the relative humidity of ambient air RH = 45 ± 10%. MilliQ water was used as a test liquid in all atomization studies.

Droplet size analysis allowed to obtain the volumetric distribution in the range of 0.1-900 μm and to find the basic numerical parameters of this distribution, i.e. the percentiles ( $Dv10$ ,  $Dv50$  = median diameter,  $Dv90$ ) and the width of the distribution defined by span  $S$ :

$$S = (Dv90 - Dv10) / Dv50 \quad (1)$$

An additional parameter included in the analysis is the percentile of droplets considered optimal in the inhalation drug delivery – the FPF i.e. fine particle fraction (European Pharmacopeia, 2017). Considering the data that may be obtained from the laser diffraction analysis, the FPF was evaluated as the volumetric fraction (equivalent to the mass fraction) of droplets smaller than 5.4  $\mu\text{m}$ .

## 2.2. Aerosol velocity field determination by Laser Doppler Anemometry (LDA)

The flow field of aerosol cloud emitted from the nebulizers was measured using 2D Laser Doppler Anemometry (2D LDA - Dantec Dynamics A/S, Denmark) with the automatic traverse system (positioning accuracy of 10  $\mu\text{m}$ ). The device was scanning the continuously released aerosol cloud along the (Z, Y) plane in 25 nodes of the rectangular mesh – Fig. 3. In such configuration the symmetry of the cloud in the third direction (X) was assumed. Due to the complexity of the experimental setup, LDA measurements could be done only for the nebulizers operated without additional airflow. At least 1000 samples at each position (node) was acquired by the system to obtain the required statistics of the mean local velocity vector. In addition, the measurement for each nebulizer was duplicated and the obtained velocity fields were averaged.

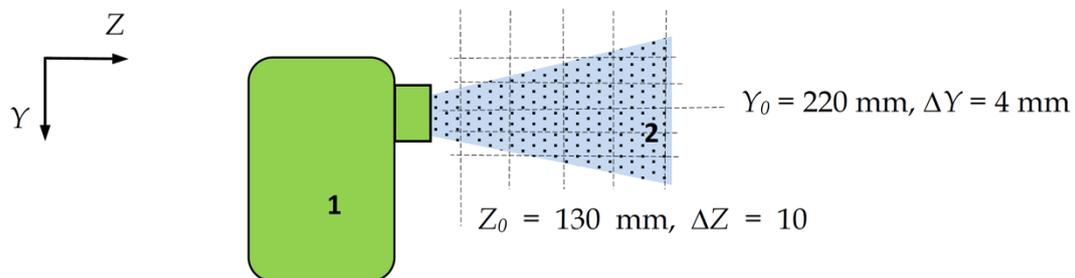


Fig. 3. The schematic of the 2D mesh in LDA measurements: 1 - nebulizer, 2 - aerosol cloud

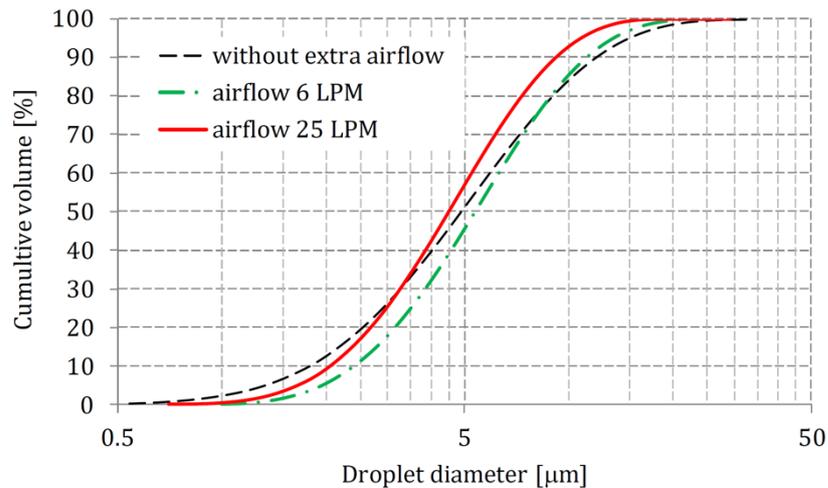
## 3. Results and discussion

The dependence of droplet size distribution on the airflow rate through the nebulizers is shown in Figure 4. Numerical data of characteristic measures of DSD are listed in Table 1.

The basic difference in aerosol characteristics obtained from both nebulizers is that DSD of the aerosol clouds generated in PN is wider than in VM ( $S = 1.6\text{-}2.1$  and  $1.1\text{-}1.35$ , respectively). PN produces a noticeable amount of submicrometer-size droplets while only a small fraction of such droplets can be detected in the aerosol generated by VM. The size of largest droplets in the aerosol emitted from both atomizers is similar, in the range of 10-20  $\mu\text{m}$ . It is assumed that the aerosol emitted from nebulizers with no additional airflow is composed of droplets suspended in the air at the saturation conditions of humidity ( $\text{RH} = 100\%$ ).

Upon mixing with the external air, the median droplet size in PN increases at the airflow rate of 6  $\text{dm}^3/\text{min}$  (from 4.9  $\mu\text{m}$  to 5.4  $\mu\text{m}$ ). However,  $Dv50$  becomes significantly smaller (4.5  $\mu\text{m}$ ) when the extra airflow is high (25  $\text{dm}^3/\text{min}$ ). It seems that addition of moderate amounts of external air cause the evaporation (disappearance) of the smallest droplets with rather a small effects on the larger ones. This is confirmed by the values of  $Dv10$  (increase from 1.8  $\mu\text{m}$  to 2.4  $\mu\text{m}$ ) and  $Dv90$  (reduction 12.0  $\mu\text{m}$  to 11.2  $\mu\text{m}$ ). However, when dilution with external air is high (25  $\text{dm}^3/\text{min}$ ), evaporation of the biggest droplets is also visible ( $Dv90$  decreases to 9.15  $\mu\text{m}$ ) which results in the reduction of the median diameter  $Dv50$  of droplets in the cloud. These observations can be easily explained on the theoretical ground. When large volume of ambient air with low humidity is mixed with the wet cloud, this dilution reduces the vapor concentration in the gas phase, therefore builds the concentration gradient required for evaporation of water droplets. The smallest droplets evaporate faster (according to the square-law, Hinds, 1999), therefore they simply disappear from the cloud. When aerodynamic effects are more intense (especially at 25  $\text{dm}^3/\text{min}$  of additional air flow), this helps to obtain a better heat and mass transfer conditions increasing the evaporation rate. However, the reduction of the span with increasing

(a)



(b)

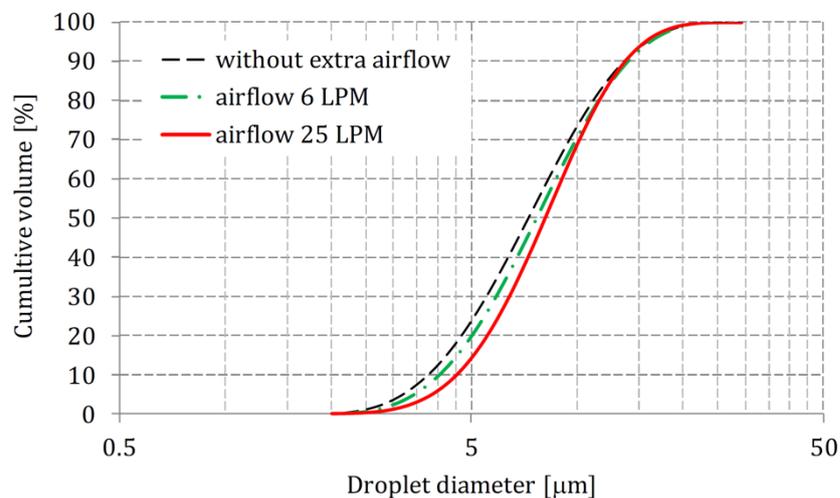


Fig. 4. The cumulative volume distributions of droplets emitted from the nebulizers after mixing with additional air (extra flow): a - pneumatic nebulizer PN (PARI), b - vibrating mesh nebulizer VM (INTEC). LPM denote litres per minute =  $\text{dm}^3/\text{min}$

dilution (from  $S \approx 2.1$  to  $S \approx 1.6$ ) illustrates the narrowing of the size distribution mainly due to evaporation of the smallest droplets.

Surprisingly, results observed in the aerosol generated from mesh nebulizer are not the same as for PN. The median droplet diameter  $Dv50$  successively increases when the extra air is mixed with the wet aerosol (from  $7.3 \mu\text{m}$ , through  $7.65 \mu\text{m}$  to  $8.1 \mu\text{m}$  at the external airflow 0, 6 and  $25 \text{ dm}^3/\text{min}$ , respectively). This may be attributed to the complete evaporation of the smallest droplets (note that  $Dv10$  increases from  $3.8 \mu\text{m}$  without an extra airflow via  $4.05 \mu\text{m}$  at  $6 \text{ dm}^3/\text{min}$ , to  $4.6 \mu\text{m}$  at  $25 \text{ dm}^3/\text{min}$  of the extra flow) with no visible effect on large droplets ( $Dv90$  remains nearly constant  $\sim 13.6\text{-}14 \mu\text{m}$ , independently on the dilution). The presence of large droplets in diluted aerosol may also be a result of the coalescence of medium-sized droplets in the turbulent flow (Podgórski et al., 2006). The size distribution becomes slightly narrower ( $S$  decreases from 1.35 to 1.12) mainly because of the disappearance (evaporation) of the smallest droplets.

Changes in DSD have further consequences for the overall quality of the aerosols in the view of their potential applications. For instance, the fine particle fraction, FPF, is one of the most important parameters defining the possibility of drug penetration and deposition in the lungs during inhalation therapies. The dependence of this parameter on nebulizer operation conditions is presented in Fig. 5. It

Table 1. The basic numerical parameters of the droplet size distribution in the aerosol at various conditions of mixing

Pneumatic nebulizer (PN)	No extra airflow		Extra airflow 6 dm <sup>3</sup> /min		Extra airflow 25 dm <sup>3</sup> /min	
	average	SD	average	SD	average	SD
Dv10 [ $\mu\text{m}$ ]	1.80	0.02	2.41	0.05	2.05	0.03
Dv50 (median) [ $\mu\text{m}$ ]	4.91	0.12	5.38	0.23	4.50	0.07
Dv90 [ $\mu\text{m}$ ]	12.04	0.55	11.24	0.63	9.15	0.18
Span [-]	2.09	0.06	1.64	0.04	1.58	0.01
FPF [%]	55.11	1.38	50.48	2.77	62.17	1.00

Vibrating mesh nebulizer (VM)	No extra airflow		Extra airflow 6 dm <sup>3</sup> /min		Extra airflow 25 dm <sup>3</sup> /min	
	average	SD	average	SD	average	SD
Dv10 [ $\mu\text{m}$ ]	3.77	0.05	4.05	0.02	4.56	0.26
Dv50 (median) [ $\mu\text{m}$ ]	7.27	0.16	7.65	0.11	8.10	0.43
Dv90 [ $\mu\text{m}$ ]	13.61	0.4	13.96	0.3	13.62	0.78
Span [-]	1.35	0.02	1.30	0.02	1.12	0.30
FPF [%]	28.56	1.14	24.62	0.59	18.56	3.27

is clearly seen, that after dilution of raw aerosol with the ambient air, the FPF obtained in the vibrating mesh nebulizer is reduced from almost 30% (no dilution) to slightly below 20% (dilution by the airflow of 25 dm<sup>3</sup>/min). It means that the effective mass of drug delivered to the lungs in reality may be reduced below the value expected from the initial DSD of aerosol generated by the nebulizer. The situation is different for pneumatic nebulizer where the strong addition of external air increases the FPF to more than 60% (with approximately 55% in the raw aerosol). In this case, dilution enhances the capability of aerosol targeting to the lungs.

Additional information on these processes can be deduced from LDA results which show the vectors of droplet velocity [ $v_x$ ,  $v_y$ ] in the cloud emitted from the nebulizers (Fig. 6).

It can be noted that PN generates droplets with a higher momentum, with the maximum velocity of approximately 1.2 m/s in the plane aligned with the outlet from the device, and approximately 0.7 m/s in the parallel plane at 40 mm distance from this outlet (Fig. 6a). The aerosol cloud is almost unidirectional, symmetric and has a width (diameter) exceeding 20 mm. In this wide and fast-moving

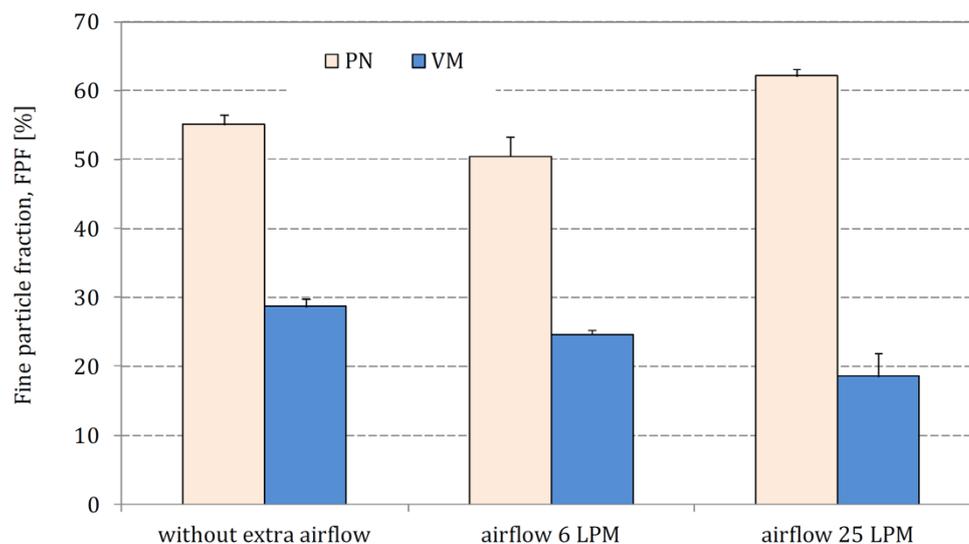


Fig. 5. Changes of fine particle fraction FPF as a function of dilution of aerosol emitted from tested nebulizers. Error bars show the standard deviation (n=3). LPM denote litres per minute = dm<sup>3</sup>/min

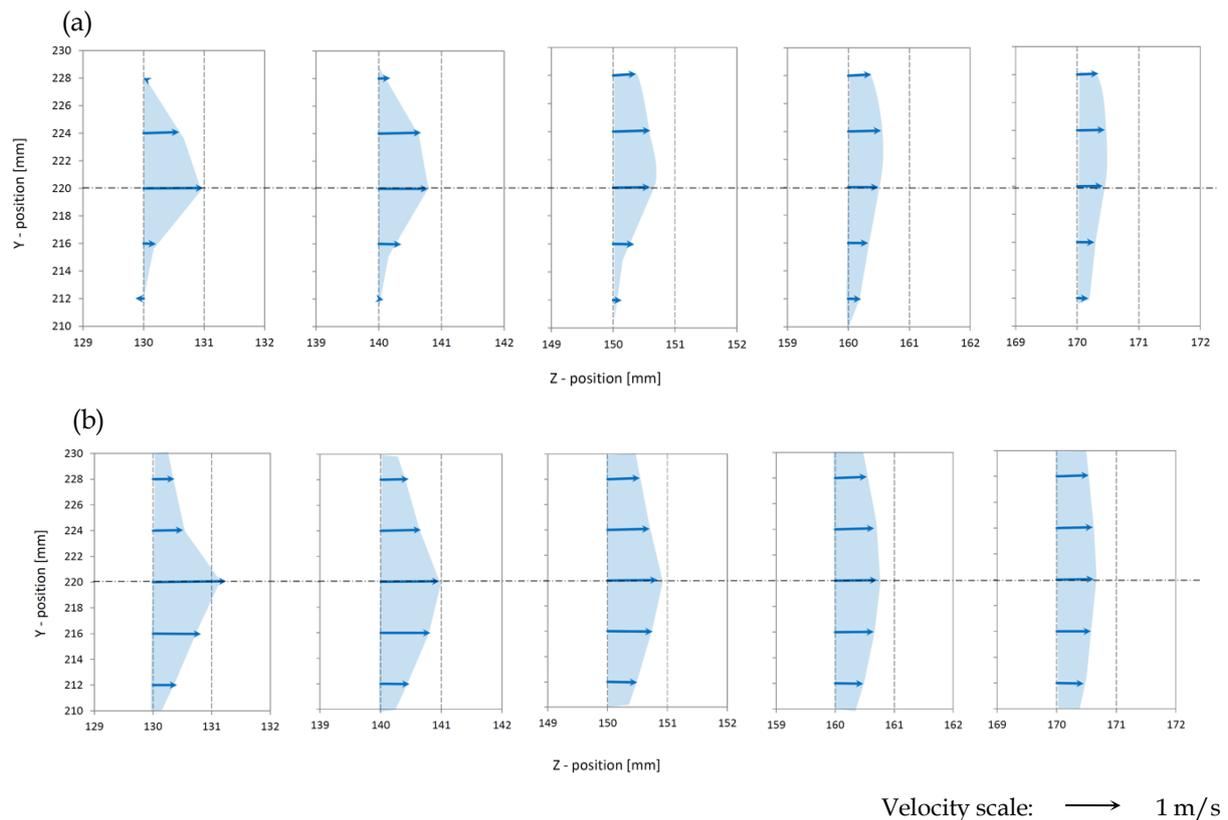


Fig. 6. Profiles of droplet velocity at the nebulizer outlet: a – pneumatic nebulizer PN (PARI), b – vibrating mesh nebulizer VM (INTEC)

cloud, the smallest droplets that are present near the cloud boundaries are probably more sensitive to the dilution with external air which allows their quick evaporation.

In contrast, the jet obtained from VM nebulizer is more centrally focused at the outlet from the device (jet diameter  $\sim 10$  mm) and develops to a wider cloud at 20-40 mm from the nebulizer outlet (Fig. 6b). Droplet velocity decreases from 1 m/s (the maximum value at the outflow plane) to 0.2-0.5 m/s in the 40 mm distance from the nebulizer outlet, so the cloud moves slower comparing to the PN. It means that droplet concentration in the central part of this cloud is also higher than in the aerosol emitted from PN. The properties of this conical cloud should facilitate the process of droplet coalescence allowing to retain the fraction of large droplets on approximately the same level, regardless their simultaneous evaporation (Podgórski et al., 2006). This helps to explain differences in the evolution of DSD in both nebulizers.

#### 4. Conclusions

Different properties of aerosol clouds are obtained during the nebulization processes, depending on the atomization method (principle) and the history of aerosol mixing with the ambient air. As shown by LDA measurements, aerosol cloud emitted from the pneumatic nebulizer is wider and faster than the cloud produced by vibrating mesh device that is expanding and slowing down a few centimetres from the nebulizer outlet. These differences in aerosol cloud geometry have consequences on the droplet size evolution after aerosol mixing with the external air. The information of this process is crucial, for instance, in the predicting droplet penetration and deposition in the lungs during inhalation, but also in the assessment of the performance of medical nebulizers. These devices are designed to maximize the mass of emitted droplets within the optimal size range of 1-5  $\mu\text{m}$ . However, as shown by this study, the effective size of droplets may be changed due to mixing with the ambient air that is usually inhaled together with the aerosolized drug. This can reduce the fine particle fraction, i.e. the amount (mass) of droplets that are more advantageous as drug carriers targeting the lower respiratory tract. Such an effect was clearly demonstrated for vibrating mesh nebulizer studied here.

Changes in the droplet size distribution are caused both by the evaporation of the smallest droplets and the coalescence of the larger ones. Our results suggest that both processes are dependent on the type of nebulizer (pneumatic vs. vibrating mesh), and on the amount of air that is mixed with the aerosol emitted from a given spraying device. Although we emphasized here the importance of the evolution of DSD in the peculiar application (i.e. medical inhalations), it remains also valid in all technical systems where obtaining the precise droplet size of liquids atomized by nebulizers is decisive for the final practical outcome of the process.

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