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PHYSICOCHEMICAL ASPECTS OF NEBULISATION: AN *IN VITRO* COMPARISON OF THREE AEROSOL DEVICES TYPES

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Introduction

Recent advances in nebuliser (NEB) design have resulted in small portable devices based on a vibrating mesh (MN) or a new generation of ultrasonic NEBs (UN). Their performance is expected to enhance the efficacy of aerosol drug therapy in patient-assisted ventilation, known to be little effective[1,2], due in particular to improved drug deposition in the lungs.

Aim

To implement an in vitro model allowing us to compare four different NEBs with respect to salbutamol output and physical characteristics, namely a) pulmonary deposition, b) particle size, c) temperature changes during nebulisation, d) osmolality, and e) changes in the number of holes in the MN mesh following use.

Methods

The following NEBs were tested: 1) Sidestream Disposable (jet, JN: Fig 1), 2) Multisonic Infra Control MN81100 (ultrasonic, UN: Fig 2), 3) Aeroneb Pro (mesh, Mna: Fig 3), and 4) Aeroneb Pro single use (MNb). Salbutamol output was determined in a simple in vitro model (Fig 4) using an HPLC system. Droplet size distribution was determined with a laser granulometer. Aerosol temperature and drug solution osmolality were also measured during aerosolisation. The MNa membranes were photographed with a Colorview III camera equipped with an Olympus SZH10 lens (Fig 5-6).

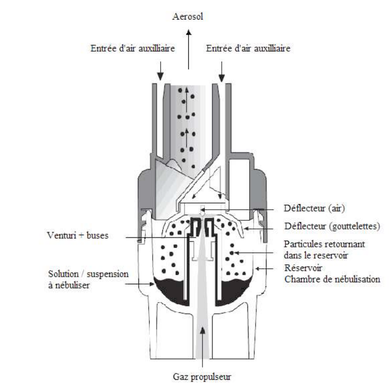


Figure 1: Sidestream Disposable® (JN), Profile Ther., UK

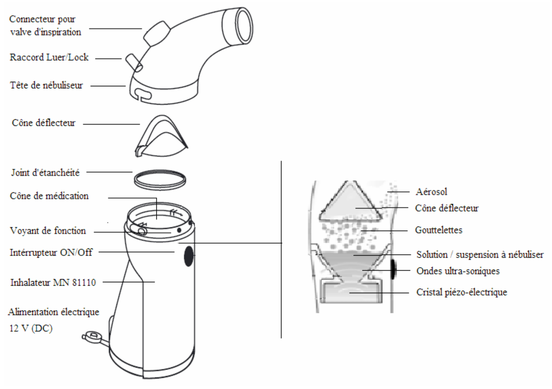


Figure 2: Multisonic Infra Control fi (UN) Schill GmbH, D

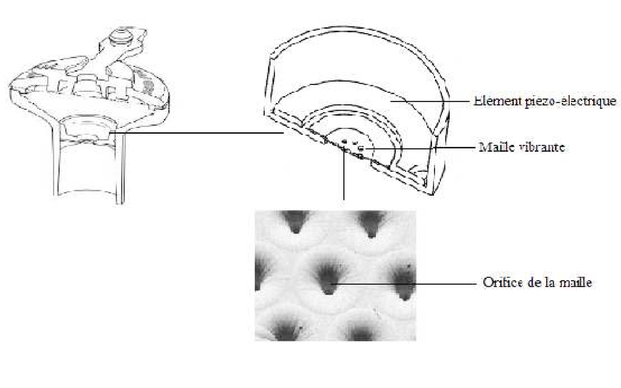


Figure 3: Aeroneb Pro® (MNa), Galway, Ireland

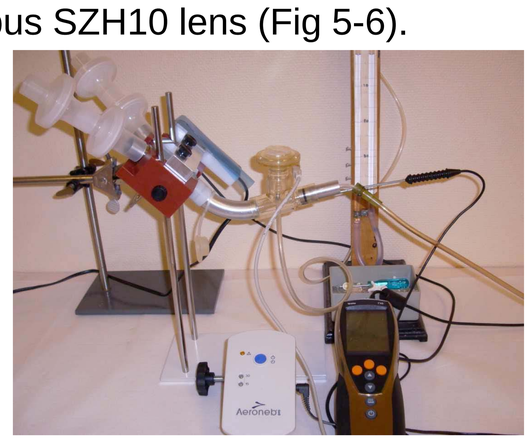
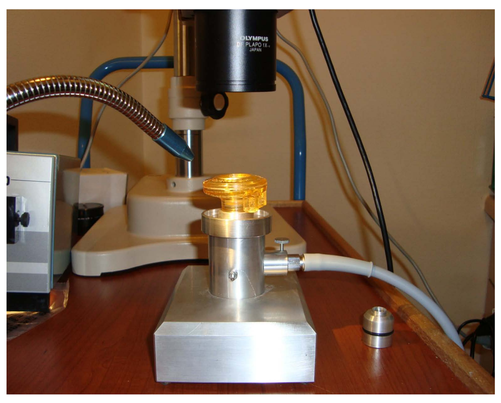
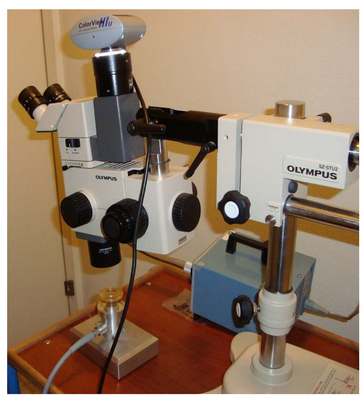
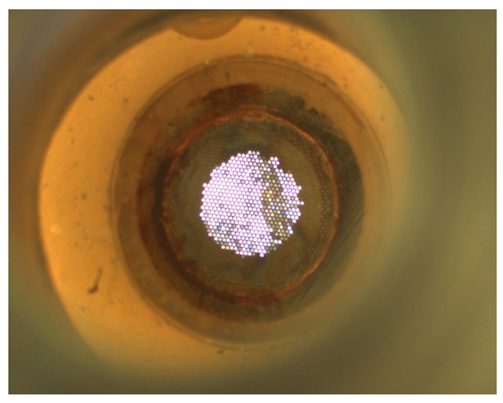


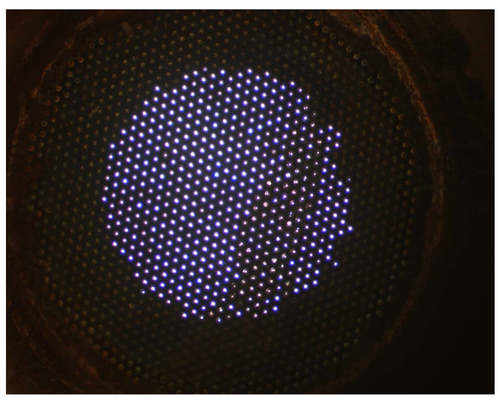
Figure 4: *in Vitro* Model with Aeroneb Pro ®





Figures 5-6 : Assembly for the realisation of photos





Figures 7-8 : MNa's membrane photographed with an Olympus microscope (increase1.5x and 2.5x)

Results

	SALB deposition (%)	Osmolality [mOsm/kg]	Variation T° [°C]	Particle Size [µm]	Number of holes
Multisonic (UN)	48.4±7.6*	379.0±33.8	+8.2±1.7	5.8±0.09	
Sidestream (JN)	27.5±4.9**	452.7±29.8	-13.9±1.3	5.0±0.14	
Aeroneb Solo (MNb)	78.8±6.5	290.3±3.8	-15.8±0.9	4.6±0.23	
Aeroneb Pro (MNa)	74.6 ±11.3	294.7±2.9	-15.8±1.2	5.1±0.22	before use: 641±58 after use: 454±36***

(± SD, n=5), *p<0.001 (vs MNb and MNa), **p<0.001 (vs MNb, MNa and UN), ***p<0.05 (vs before)

Salbutamol output was 1.8 and 2.7 times higher with the UN and MN devices compared to the JN. Particle size was significantly higher with the MN. Temperature decreased during nebulisation when the MN and the JN were used, but it increased with the UN. Osmolality of the drug solution was stable during nebulisation with the MN but increased with the UN and the JN, indicating an evaporation of the solvent. The number of holes decreased significantly with the MNa after 2 months of use (Fig 7-8), which could result in a decreased quality of droplets.

Conclusion

The in vitro model appears effective in comparing nebuliser types. Nevertheless, the differences in efficiency and physical features observed in vitro will have to be complemented by clinical trials to validate the in vitro model, recommend its routine use, and define dosage adaptations.

References

1. Di Paolo ER et al. *In vitro evaluation of bronchodilator drug delivery by jet nebulization during pediatric mechanical ventilation. Pediatr Crit Care Med. 2005; 6 (4): 462.*
2. Dautzenberg B, Diot P. *L'aérosolthérapie par nébulisation, 2e éd. Paris: Margaux Orange. 2006; p. 17.*