Efficiency of Valved Holding Chambers: Experimental Full Dose Assessment

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Introduction / Objectives

- The **Valved Holding Chamber** (VHC) devices are used by patients **without** the **capacity to** properly **use** a pressurized Metered-Dose Inhaler (pMDI).
- VHC devices contribute to the **reduction** of the **oropharyngeal** spray **deposition**, while allowing the patient to **breathe normally**.
- The main objective is to experimentally **evaluate** eight commercially available VHC devices, through **two** distinct **Systems**.
- VHC efficiency was evaluated through the assessment of the **Emitted Dose**.

Methods

Devices

The experimental tests were performed using a commercial pMDI HFA-134a containing a Salbutamol formulation (**Ventolin®** from GlaxoSmithKline®) coupled with the **VHC device**. A total of 8 devices were assessed throughout this experimental study (see **Figure 1**).

(a) A2A Spacer® from Clement Clarke International®, *(b)* AeroChamber Plus® from Trudell Medical International®, *(c)* Volumatic® from Glaxo SmithKline®, *(d)* NebuChamber® from AstraZeneca®, *(e)* SpaceChamber Plus® from Medical Development International®, *(f)* Vortex® from PARI®, *(g)* Compact SpaceChamber Plus® from Medical Development International® and *(h)* OptiChamber Diamond® from Philips®.

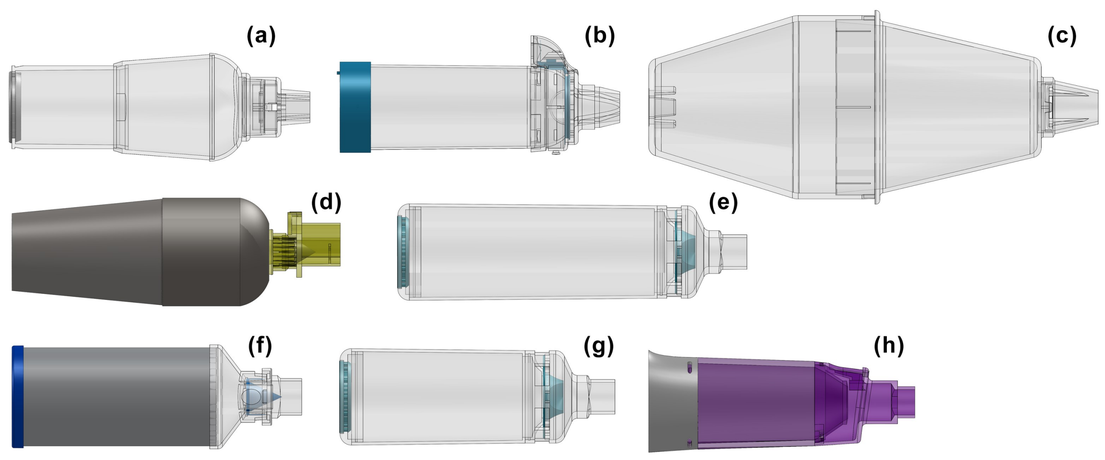

Figure 1. Geometric representation of the VHC devices evaluated.

Experimental System

Figure 2 depicts that the pMDI and the VHC were attached to a rubber adapter, fitted on the edge of an aluminum filter housing (containing a paper filter MN 1674 from Macherey-Nagel).

In **System 1**, this component was then coupled to a vacuum pump, which was calibrated to an output of 26 L/min. A flow meter was used to monitor the vacuum pump flow rate, which was controlled by a needle valve.

In **System 2**, the filter housing is directly connected to a breath machine, which is based in a closed-form cam-follower mechanism.

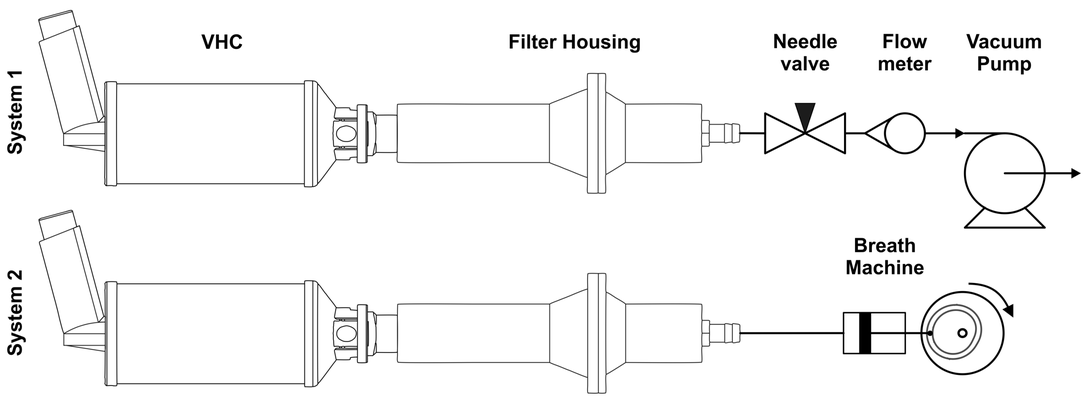

Figure 2. Schematic representation of the experimental systems.

Breath Profile

A 7 yrs. old asthmatic child breathing profile was considered to be the study target, which was applied in the breath machine of **System 2**. The profile was defined by several literature data sources, along with a sinusoidal simplification: breathing frequency of **30 BPM**, duty cycle of **0.33** and tidal volume of **150 mL**. The breath profile used is represented in **Figure 3**.

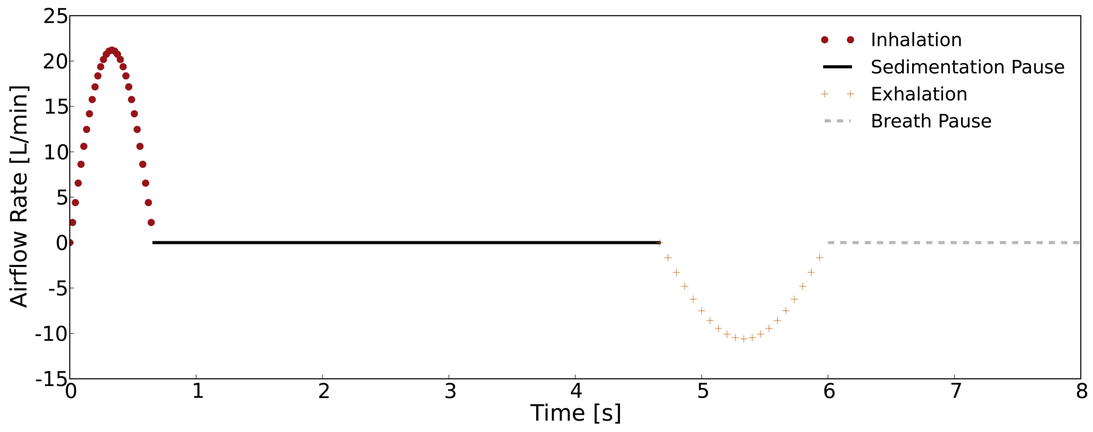

Figure 3. Asthmatic breath profile used in the experimental System 2.

The amplitude of the inspiratory sinus is **21 L/min**. A pause of 4 s after inspiration was added, to **allow** for the **sedimentation** of drug **particles** in the **lungs**. After the exhalation phase, a 2 s pause was intended to **simulate** the **poor coordination** of an asthmatic patient using a VHC device.

Methods (cont.)

Experimental Protocol

1. VHC devices were **submerged** in an anionic soap solution (1:250) for a period of 1h and **dried** for at least 12h, prior to the experimental procedure.
2. The pMDI canister was then **shaken** for 5 seconds and **fired** twice **to waste** in its original actuator. The canister was then placed in the **service actuator**, already **attached** to the VHC.
3. In **System 1**, a total of 20 puffs were **discharged**, with **shaking** of the canister for 5 seconds **between each** puff.
4. Prior to **shutting off the pump**, it was allowed a 30 seconds suction time starting from the last puff.
5. In **System 2**, the actuations were made at the **beginning** of the **inspiratory phase** during 20 cycles, **shaking** the canister between puffs.
6. A minimum of 3 repetitions of each test **were made**, in order to **reduce protocol errors** and increase the result's significance.
7. Every **stage** of the System was **washed**, with NaOH 0.01M, into **volumetric flasks**: primarily, the **pMDI actuator** into a 25 ml flask, then the **VHC** device into a 100 ml flask and, finally, the **paper filter** and the **filter housing** into 50 ml flasks.
8. To improve the drug solubility and its release from the paper filter, the solution was initially placed into an ultrasonic shaker for 10 min.
9. The washing solutions **absorbance** (λ = 244 nm) was **measured** in triplicate by means of a **UV-Vis spectrophotometer** (UV-2401PC from Shimadzu Corporation®).
10. Using a **calibration curve** of **known** absorbance for specific **concentrations** of **Salbutamol**, the washing solutions concentration was **estimated**, which allows the **determination** of **mass** retained in each stage.
11. Values of the **total mass collected** in each test were also **determined** and used to **evaluate** the **accuracy** of the test. **Only** tests with mass recovery **between** 85% and 120% of the mass injected were considered as **valid**.

Results

Table 1 reports the experimental values obtained for **System 1** (i.e. at 26 L/min) and **System 2** (i.e. using a Breath Profile). Data is presented in terms of **Emitted Dose** (Ex-actuator) considering a dose base of 100 mcg salbutamol.

Table 1. Experimental data obtained for each VHC device.

VHC Device *(Acronym)*	**Emitted Dose** *(Ex-actuator)* **[mcg]**	
	26 [L/min]	**Breath Profile**
Volumatic® *(VOL)*	32.2 ± 2.4 (n=3)	16.1 ± 0.6 (n=3)
Compact SpaceChamber Plus® *(CSCP)*	36.8 ± 0.2 (n=3)	23.0 ± 1.2 (n=3)
A2A Spacer® *(A2A)*	38.1 ± 2.9 (n=3)	10.5 ± 1.1 (n=3)
OptiChamber Diamond® *(OCD)*	40.7 ± 0.6 (n=3)	20.8 ± 0.3 (n=3)
SpaceChamber Plus® *(SCP)*	41.9 ± 1.8 (n=4)	24.3 ± 0.4 (n=3)
NebuChamber® *(NC)*	46.3 ± 2.3 (n=4)	21.6 ± 0.8 (n=3)
AeroChamber Plus® *(ACP)*	46.9 ± 0.7 (n=3)	21.4 ± 0.1 (n=3)
Vortex® *(V)*	50.8 ± 1.8 (n=4)	18.2 ± 0.9 (n=4)

Figure 4 depicts the results reported in **Table 1**, sorted in ascending order of Emitted Dose at 26 L/min.

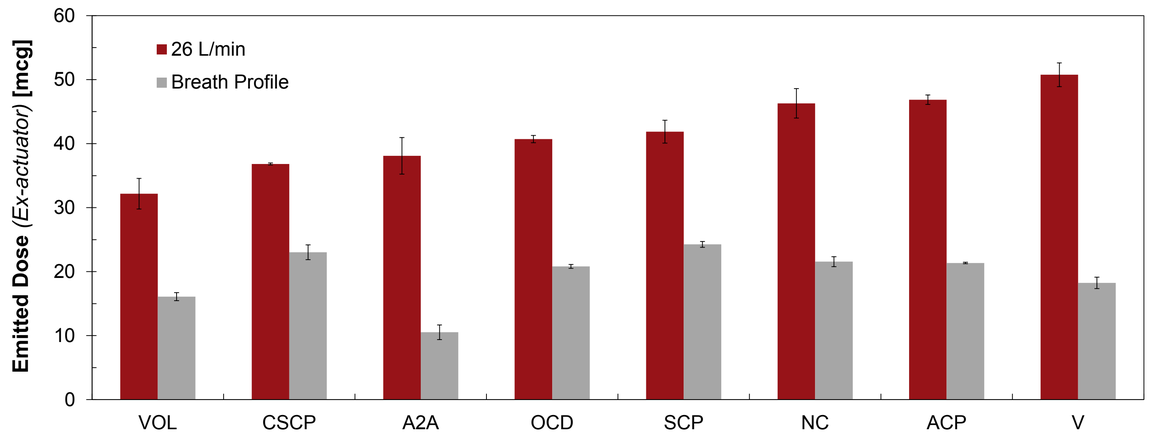

Figure 4. Graphical representation of the Emitted Dose (Ex-actuator) for the evaluated devices, on both systems.

- The result reported reveals that **V** has the **highest** Emitted Dose of the VHC at constant flow. Under the use of a unsteady flow the **SCP** is the device with **highest** Emitted Dose.
- **Ranking** as:
  System 1: VOL < CSCP < A2A < OCD < SCP < NC < ACP < V
  System 2: A2A < VOL < V < OCD < ACP < NC < CSCP < SCP
- **Vortex** is the **best** device at **constant flow** although the same **is not** verified under **unsteady flow**.
  This may arise from valve leakage.
- **Longer VHC** body results in **higher** Emitted Dose.
  This can be concluded from comparing SCP with CSCP.
- Emitted Dose at unsteady flow is **1.6 – 3.6** times **lower** than at constant flow.
  Anti-static materials play a major role as the plume is on hold in the VHC body for a longer period.

Conclusions

- Considering Emitted Dose results, the **Vortex** is the **best** VHC device at **constant flow** and the **SpaceChamber Plus** at **unsteady flow**.
- Body **length**, valve **design** and device **material** seems to be the **most** influential design characteristics.

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Funding

Centre for Mechanical and Materials Technologies

FCT Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA EDUCAÇÃO E CIÊNCIA