Inhaler Performance at High Altitude

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Introduction

Dry powder (DPIs) and pressurized metered dose (pMDIs) inhalers must operate reliably in a variety of environments and are typically only tested near laboratory conditions. Little is known about device performance at reduced pressure associated with high altitude [1,2]. Testing was conducted to determine the in vitro lung dosage of a variety of different inhaler devices at a number of different altitudes. The data collected provides a good relative understanding of how the dosing of inhaler devices will change with altitude.

Method and Materials

- **pMDI Testing**
  - Data for five devices, Symbicort®, Airomir™, Ventolin®,QVAR™, and Apo-Salvent, were collected at elevations of 670m, 2450m, 3260m, and 4300m. Properties of the inhalers are given in Table 1.
  - A constant inspiratory flow rate of 30 L/min was used at all locations.
  - The flow profile consisted of an initial 0.5 s period to allow for the flow stream to become uniform, followed by one actuation and a 6 second inhalation period, resulting in a total volume of 3 liters.

- **DPI Testing**
  - Data for two devices, Turbuhaler® and Ventolin® Diskus®, were collected at elevations of 670m, 2450m, 3260m, and 4300m. Properties of the inhalers are given in Table 1.
  - Since breathing profiles of patients inhaling from a DPI at reduced ambient pressure are unknown, two possible scenarios were tested:
    - **Matched Flow Rate**
      - The volumetric flow rate was kept the same for all altitudes for each device.
      - A constant inspiratory volume of 2.4 liters was used.
    - **Matched Pressure Drop**
      - The pressure drop across each device at each altitude was kept constant at 4kPa.
      - Resistance of each device was expected to change with altitude and thus the volumetric flow rate changed.
      - As the flow rate changed, with a 3 liter inhalation volume, the length of each test changed.

- Test conditions were maintained at 22 ±1.7 °C, 49.3 ± 9.2 %RH. For simulation of aircraft cabin conditions silica gel dried air was used.

<table>
<thead>
<tr>
<th>Product</th>
<th>Propellant</th>
<th>Labeling (mg)</th>
<th>Format</th>
</tr>
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</table>

**Results**

- **pMDI shot weight and in vitro lung dose are unaffected by altitude**

- **DPI show device dependent reduction in in vitro lung dose for matched volumetric flow rate**

- **DPI device resistance is a function of ambient pressure**

**Conclusion**

Collected data for most of the devices tested displayed little effect of altitude on measured in vitro lung dose. Note: The effect of reduced pressure on particle size distribution of the delivered aerosol was not tested in this study.

- All pMDIs tested delivered as in vitro lung doses that were within ±20% of nominal dosage bands.
- Ventolin® Diskus® displayed very consistent in vitro lung dose at all conditions tested.
- Bricanyl Turbuhaler® was unaffected by altitude when tested under matched pressure drop conditions.
- Bricanyl Turbuhaler® in vitro lung dose displayed a negative correlation with altitude when tested under matched flow rate.
- All pMDIs tested had consistent dosage when aircraft cabin conditions were simulated.
- Spray duration and shot weight of all pMDIs was unaffected by altitude.
- The device resistance of DPIs is affected by ambient pressure.

**Table 1: Important properties of inhalers tested.**

- **Absolute in vitro lung doses of pMDIs**

- **In vitro lung dose for matched pressure drop**

- **DPI device resistance, R, as a function of ambient pressure, P:**

\[
R(P) = R_0 \left( \frac{P}{P_0} \right) \quad P_0 = \text{Standard pressure, } 100 \text{kPa (± sea level), } R_0 = \text{Device resistance at standard conditions.}
\]

**References**


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