

Varsha Chavan, Ph.D.

Thesis Abstract (2001)

USE OF SIMULATED INHALED VOLUMES, FLOW RATES AND FLOW RATE RAMPS TO EVALUATE *IN VITRO* DRY POWDER INHALER PERFORMANCE

Dry Powder Inhalers (DPIs) utilize a patient's inspiratory maneuver to entrain and deaggregate a powder forming an inhalation aerosol. United States Pharmacopeia (USP) DPI methods replicate the peak rate a patient might achieve, but do not account for how this peak is approached. This research developed a simple, robust system to simulate different rates of rise (ramps) to a final peak inspiratory flow rate. Ramps were programmed to reach 30, 60, 90 and 120 L/min over 100 ms, 500 ms, 1, 2 and 3 s. Using this computerized system, it was demonstrated that peak flow rate, the rate at which that flow rate was achieved and carrier particle size, influenced powder emptying from three passive DPIs. Generally, powder emptying increased as ramp steepness increased - this being most evident at 30 L/min. Greater emptying was usually facilitated by larger carrier particles using all ramps and peak flows. The USP method of instantaneous peak flow rate generation produced more emptying than even the steepest ramp, and may therefore overestimate powder emptying during use. While maximized powder emptying is a prerequisite of optimized dose delivery, a meaningful determination of Fine Particle Fraction (FPF), the fraction of the aerosolized output likely to reach the lungs, is more critical to therapeutic outcome. A semi-automated system was developed permitting ramped air flow through a DPI while maintaining a relatively constant air flow through an inertial impactor. This system suggested that a steeper rate of rise in air flow elicited a higher FPF compared to a shallower ramp at test flow rates of 30 and 60 L/min. FPF determined by the USP method was higher than the ramp method at these flow rates. There were no significant differences in FPF when a 2 and 4 L inhaled volume were compared. This research highlighted the limitations of two existing compendial tests when applied to therapeutic aerosols generated from DPIs, and provides a basis and apparatus for evaluating in vitro DPI performance more realistically. It also illustrates the potential dangers in using in vitro tests to infer in vivo performance in the absence of valid correlations.

Education Summary

- Aug.1995 - 2001: Graduated with Ph.D. in Pharmaceutical Sciences, University of Maryland.
- Aug.1990 - Aug.1994: B. S. in Pharmacy, University of Bombay, Prin. K. M. Kundnani College of Pharmacy, India. Graduated with a Distinction grade (top 5% of the class).

Employment Summary

- Mar. 2001 - present: [Schering Plough Research Corporation](#), Kenilworth, NJ.

Research Experience

- Jan.1996 - Feb 2001: Research Assistant at the University of Maryland, Department of Pharmaceutical Sciences, Inhalation Aerosols Laboratory. Dissertation topic: Effect of particle size and rise in simulated inspiratory flow rate on device emptying in Dry Powder Inhalers. Familiar with the use of C++ programming for data acquisition and monitoring. Experienced in HPLC assay and method development, writing internal S. O. P.s, spectrophotometric analysis and different techniques for aerosol sizing which include the Aerosizer, Malvern, Andersen

Cascade Impactor, Single and Multistage Liquid Impinger. Hands on experience with testing and formulation of Metered Dose Inhalers and Dry Powder Inhalers.

- June 1997 - Sept. 1997: Summer intern at the Dupont Merck Pharmaceutical Company, Wilmington, Delaware. Project: To study the effect of excipients, and storage conditions on the dissolution performance of hard gelatin capsules. Worked with preformulation and formulation groups. Experienced in designing stability studies, analyzing preformulation data and handling powders for solid dosage formulations.
- Aug. 1995 - Jan. 1996: Teaching Assistant at the University of Maryland, Department of Pharmaceutical Sciences. Responsible for grading and teaching dispensing labs. Experienced with the use of word processing and spreadsheets software.
- Jan. 1995 - July 1995: Research Assistant at the University of Missouri, Kansas City, Department of Pharmaceutical Sciences. (Drug delivery Laboratory). Synthesized and analyzed antiviral compounds.
- Aug. 1994 - Dec. 1994: Intern with the pharmaceutical division at Glaxo India Limited, Bombay, India. Involved with the lab scale manufacture of aerosol formulations, oral solutions, oral suspensions, topicals, creams and ointments.

Publications

- Recommendations to the FDA: MDI Tests and Methods in the CMC Draft Guidances for MDIs and DPIs. Drug Information Journal, Volume 36, pp.549-556, 2002. ITFG/IPAC-RS Tests and Methods Technical Team: Lex Adjei, Varsha Chavan, Harris Cummings, Brent Donovan, Carole Evans, Richard Evans, Kevin Fitzgerald, Bill Gore, Kristi Griffiths, John Hart, Fiona Millar, Rajni Patel, Bjorn Persson, Nats Rajagopalan, Friedrich Schmidt, Jeff Schuster, Christopher Sciarra, Susan Sultzbaugh, Tony West, and Bruce Wyka
- Effect of Rise in Simulated Inspiratory Flow Rate and Carrier Particle Size on Powder Emptying from Dry Powder Inhalers. Varsha Chavan and Richard Dalby. AAPS Pharmsci 2000; 2 (2) article 10. (<http://www.pharmsci.org/>)
- Evaluation of Aerosol Drug Output from the OptiChamber and AeroChamber Spacers in a model system. Richard N. Dalby, Shailaja Somaraju, Varsha S. Chavan, and Dayna Jarvis. Journal of Asthma, 35 (2), 173-177 (1998).
- Evaluation of Aerosol Drug Output from Ventilator Circuits fitted with the Optivent and Aerovent in-line Spacers. Richard N. Dalby, Rajkumari N. Jashnani, Dayna Jarvis and Varsha S. Chavan. Proceedings of Respiratory Drug Delivery VI, Interpharm Press, USA, pp 299-301 (1998).

Abstracts and Presentations

- Performance of a dry powder inhaler under different inhaled volumes and rates of rise in simulated inspiratory air flow. Varsha Chavan and Richard Dalby. Abstract accepted to be presented as a poster at the American Association of Pharmaceutical Scientists Conference, October 2000.
- Effect of particle size and rise in simulated inspiratory flow rate on device emptying in a dry powder inhaler system, Varsha Chavan and Richard Dalby. Poster at the American Association of Pharmaceutical Scientists Conference, November 1999.
- Effect of rise in simulated inspiratory flow rate on device emptying in dry powder inhalers, Varsha Chavan and Richard Dalby. PharmSci, 1 (1), S-213, November 1998.
- Performance of a reformulated albuterol metered dose inhaler in the presence and absence of a spacer, Varsha Chavan and Richard Dalby. Pharmaceutical Research, 14 (11) S-144, September 1997.

- In vitro metered dose inhaler performance: An accelerated stability study comparing levalbuterol sulfate and Ventolin. Richard Dalby, Dudley Demarest, R. Gary Hollenbeck, James Leslie, Martin Redmon, Stephen A. Wald, Varsha Chavan, Dayna Jarvis, Rajkumari Jashnani, Doungkamol Leaokittikul, Shailaja Somaraju and Julie Suman. *Pharmaceutical Research*, 14 (11), S-136, September 1997.
- Comparison of two particle sizing methods for an accelerated stability study of metered dose inhalers. Rajkumari Jashnani, Varsha Chavan, Richard Dalby, Dayna Jarvis, Doungkamol Leaokittikul, James Leslie, Bipin Mistry, Martin Redmon, Shailaja Somaraju and Linda Wong. *Pharmaceutical Research*, 14 (11), S-146, September 1997.
- Effect of excipients and storage conditions on the dissolution performance of hard gelatin capsules. Poster and podium presentation at the DuPont Merck Pharmaceutical Company, Wilmington, Delaware. August 1997.
- Relationship between aerosol particle size and dose emitted from a spacer device. Philadelphia Pharmaceutical Forum, King of Prussia, PA. March 1997.
- Effect of spacer type on fine dose fraction emitted from a Ventolin MDI sized by the single stage liquid impinger, demonstration for the Inhalation Aerosol Technology Workshop, Baltimore, MD. June 1996.

Honors and Awards

- Recognized for organizational and leadership skills (Chair, Fund Raising and Treasury) at GRASP 2000 (Graduate Research Association of Students in Pharmaceutics) held in Baltimore, June 2000.
- Runners-up award in the best poster-Pharmaceutical Sciences category at the inter-campus Graduate Research Conference, April 2000.
- Best Podium Presentation Award in Pharmaceutical Sciences at the campus wide Graduate Student Research Day, April 1999.
- Member of the Rho Chi National Pharmacy Honors Society, inducted in 1997.
- Recognized as a University Student Leader in the University Student Government Association and the International Student Organization, 1999.

Professional Affiliations

- American Association of Pharmaceutical Scientists (AAPS)
- Rho Chi Honors Society
- Pharmaceutical Graduate Student Association
- Kappa Psi Professional Pharmaceutical Fraternity

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