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Thesis Abstract (2002)

DEVELOPMENT OF A PATIENT INHALATION TRAINING TOOL AND USE OF SIMULATED INHALATIONS TO STUDY DRY POWDER INHALER PERFORMANCE REALISTICALLY *IN VITRO*

Patients find metered dose inhalers difficult to use correctly. A computerized training tool to detect and immediately respond to common problems, such as, inadequate coordination between inhalation and actuation, was developed. Pressure, force and acceleration transducers mounted on a placebo MDI, and a C program written to acquire these signals, was used to deliver situation-specific, real time feed back on the performance of five volunteers. A computer interface provided pop-up instructions in response to the volunteer's inhalation profile, actuation force, shaking intensity and their temporal relationship. Improvements in technique were realized, and the system proved capable of recording inspiratory profile parameters.

A method of reproducing recorded inhalation profiles was validated, and applied to in vitro testing of a Rotahaler dry powder inhaler. The performance of passive DPIs is known to be dependent on inhalation profile, but clinical studies have little power to discriminate the influence of specific breathing patterns on lung deposition. An electronic valve and computerized control system were used to generate a series of simulated inhalation profiles. Four liters of air, at a peak flow rate of 30, 60 or 100 L/min, was drawn through a preloaded Rotahaler. Peak flow was achieved instantaneously (USP method) or linearly approached over 0.1, 0.5, 1, 2 or 3 seconds. The amount and particle size of albuterol and lactose exiting Rotahaler was simultaneously determined by laser diffraction and inertial impaction. Rapidly imposed, higher flow rates drawn through the DPI induced more emptying and smaller emitted drug and carrier particles sizes. The USP method of instantaneously reaching the peak flow rate yielded maximal powder emptying and minimum particle size. Area under the laser obscuration versus time plot was found to correlate to total powder emptying. This relationship was used to demonstrate that most powder leaves a DPI before the peak flow rate is achieved. A correlation between the fine particle fraction of albuterol (obtained from cascade impaction) and the volume mean diameter (of lactose and albuterol) obtained from laser diffraction was established. This work represents a step towards applying realistic inhalation profiles to both established inertial, and more convenient laser based aerosol evaluation techniques.

Education Summary

- Aug. 1997 - April 2002, Ph.D. in Pharmaceutical Sciences, University of Maryland.
- Aug. 1995 - Aug. 1997, M.S. in Chemistry, Department of Chemistry, Indiana State University.
- Aug. 1984 - Aug. 1989, B.S. in Chemistry, School of Pharmacy, Beijing Medical University.

Employment Summary

- Senior Research Chemist, Inhalation Drug Delivery, 3M Pharmaceuticals.
- Jan. 1998 - Apr. 2002, Research Assistant at University of Maryland, Baltimore, Department of Pharmaceutical Sciences, Aerosols Laboratory. Experienced in HPLC assay and method development, different techniques for aerosol sizing which include the Andersen Cascade Impactor. Familiar with the use and testing of spacer devices, metered dose inhalers and dry powder inhalers. Familiar with C and C++ software, and have used them to develop programs to monitor the flow rate of patient's on a computer via a DAQ card.

- Aug. 1997 - Jan. 1998, Teaching Assistant at University of Maryland, Baltimore, Department of Pharmaceutical Sciences.
- Aug. 1995 - Aug. 1997, Research Assistant at Indiana State University, Department of Chemistry, major in bioorganic chemistry. Experienced in organic synthesis of polyamines, separation, purification, and testing as inhibitors on trypanosome. Several compounds with low Ki values were discovered.
- Aug. 1989 - Aug. 1995, Research Assistant, Department of Air and Bio-material Monitoring, Institute of Occupational Medicine, Chinese Academy of Preventive Medicine, Beijing, China. Experience with sampling polluted air from workplace atmosphere, and analysis by GC and HPLC. Method development to assay pollutants.

Publications and Presentations

- Poster at Respiratory Drug Delivery VII Symposium. **Zhili Li** and Richard Dalby, Computerized Training Tools To Help Patients Use Their Metered Dose Inhaler (MDI) Or Dry Power Inhaler (DPI) Correctly - Parameter Development, May, 2000.
- Michael Fennie,* Mary O'Sullivan, **Zhili Li** and Cyrus Bacchi, "Anti-trypanosomal Effects and Synthesis of N-(2-naphthylmethyl)-spermine Derivatives", the 219th National ACS meeting, San Francisco, CA, March 2000.
- Mary O'Sullivan, Michael Fennie,* **Zhili Li** and Cyrus Bacchi, "Inhibition of Trypanothione Reductase and Trypanocidal Effects of 2-Naphthylmethyl Substituted Polyamines", the 219th National ACS meeting, San Francisco, CA, March 2000.
- Poster at American Association of Pharmaceutical Scientists. Li, Z. and Dalby, R., Computer Assistance in Teaching Patients to Use Their Inhaler Correctly, November 1999.
- Poster at American Chemistry Society. O'Sullivan, M.C., **Li, Z.** and Hancock, M., Novel polyamine derivatives as inhibitors of trypanothione reductase and trypanocides, March 1999.
- O'Sullivan, M.C., Zhou, Q., **Li, Z.** Polyamine derivatives as inhibitors of trypanothione reductase and assessment of their trypanocidal activities. Bioorg. Med. Chem. 1997, 12, 2145.
- M. O'Sullivan, Q. Zhou and **Z. Li**, "Inhibition of Trypanothione Reductase by Spermidine and Spermine Derivatives", the 29th Annual Great Lakes Regional Meeting of the American Chemical Society, Illinois State University, Normal, Illinois, May 1996.

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