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EFFECT OF SALT SELECTION AND ENVIRONMENTAL CONDITIONS ON DRY POWDER AEROSOL GENERATION

Three salts and the free base form of micronized albuterol, with similar particle size distributions and varying solubilities, were generated and studied as aerosols from a model dry powder inhaler (DPI) using a twin stage impinger (TSI) under varying environmental conditions. Albuterol adipate diethanolate (AAD) and albuterol stearate (AST) were prepared and characterized along with albuterol (ALB) and albuterol sulfate (ASUL). The model DPI was loaded with pure micronized drug in its various forms and inserted into the TSI following pre-equilibration at 20, 30 or 45°C and 30 through 95% relative humidity (RH). After a further 3 minute re-equilibration period, drug was aerosolized by withdrawing air through the DPI at 60 L/min for 20 seconds. Washings from the DPI and TSI were analyzed by UV spectroscopy. Drug collected in stage 2 of the TSI was expressed as fine particle dose (FD) or fine particle percent of either the loaded dose (FP loaded) or the amount emitted from the DPI mouthpiece (FP emitted).

Thermal analysis showed that ALB, AAD and AST melted at 158, 182 and 116°C, respectively. ASUL decomposed at approximately 200°C. At 22°C, apparent solubilities in deionized water of ALB, ASUL, AAD and AST were 15.7, 250, 353 and 0.6 mg ml⁻¹ respectively. Using a validated rotating disk dissolution apparatus at 120 rpm, intrinsic dissolution rates of ALB, ASUL and AAD in pH 7.4 phosphate buffer at 37°C were 1.1, 20.4 and 24.0 mg min⁻¹cm⁻², respectively. A slow non-linear dissolution profile of AST was obtained under the same conditions due to the formation of a stearate-rich layer on the surface. The release rate of albuterol from AST was consistent with its possible use for sustained release in the lung following aerosol delivery.

At 20°C and 50 %RH, 40% of the loaded dose of ALB was emitted from DPI compared to 60-67% for the salts. FP emitted [mean (experimental range), n=3] were 77.7 (7.3), 63.6 (4.2), 9.0 (1.8) and 55.7 (3.4) for ALB, ASUL, AAD and AST, respectively. Emptying of the DPI was affected only in extreme environments (high temperature and RH). Increasing RH and temperature decreased FD, FP loaded and FP emitted of ALB and ASUL. These results for AAD and AST were slightly reduced at higher temperatures and humidities. While the solubilities of the various drug forms did not correlate with FD, FP loaded and FP emitted, there is clearly a need, in some circumstances, to define specific ranges of temperature and humidity for use during dry powder aerosol testing and use.

Education Summary

- Sept. 1994 - June 1996, Post Doctoral Student in Department of Pharmacy and Pharmaceutics, Medical College of Virginia at Virginia Commonwealth University working with Peter Byron.
- Aug. 1985 - May 1988, College of Pharmacy, Bombay University, B. Pharm.

Employment Summary

- Initial Employer, Dura Pharmaceuticals, San Diego, CA
Publications


Abstracts and Presentations

Professional Affiliations

• American Association of Pharmaceutical Scientists (AAPS)

Honors and Awards

• United States Pharmacopeia Fellow (1992)
• John Wood Award for Excellence in Graduate Study of Pharmaceutical Sciences, given by Department of Pharmacy and Pharmaceutics, Medical College of Virginia at Virginia Commonwealth University (1994)

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