Compounding of an oral suspension of clonidine hydrochloride 20 µg/mL for neonatal patients using tablets & a self-contained wet-milling technology

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Introduction

- For the pediatric population, oral liquids are commonly compounded from tablets using a mortar and pestle to manually grind the solids into particles of an appropriate size, prior to incorporating them into liquids
- A new automated wet-milling technology enables compounding to be performed within a self-contained single-use multipurpose plastic container. [Figure 1]
- The specialized container compounds, stores and dispenses the oral liquid with no required product transfers. All the compounding is undertaken within an enclosed environment with no loss of medication.
- The novel wet-milling process provides enhanced product physical features leading to accurate and precise dose uniformity.
- A study was undertaken using clonidine hydrochloride tablets to demonstrate the efficiency of the compounding process in formulating a low concentration formula for neonates with the required physical-chemical features and the resultant benefits for pharmacists and patients.

Methods

- Clonidine hydrochloride tablets were compounded into 20 µg/ml oral suspension preparations.
- The requisite number of tablets and specified quantity of water were placed into the specialized plastic containers.
- The containers were capped and placed inside the sealed holders within the milling unit [Figure 2].
- The specially textured container surface combined with a high RPM planetary motion from the machine results in a wet milling process that converts the contents into a fine uniform suspension. [Figure 3]
- The required amount of simple syrup was added and the product mixed by shaking. [Figure 4]
- Following compounding, the container serves the roles of storage and dispensing of the compounded product.
- Dose uniformity and chemical stability studies were undertaken using HPLC methods.

Equipment and Materials

Figure 1: Enclosed wet milling device that produces uniform particles leading to palatable high-quality liquid formulas with the required dose uniformity

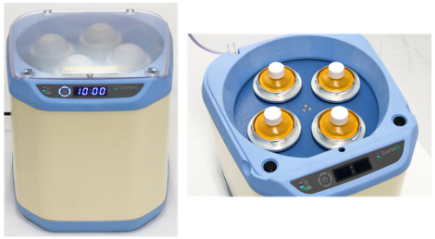

Figure 2: Milling unit closed and opened showing containers in place

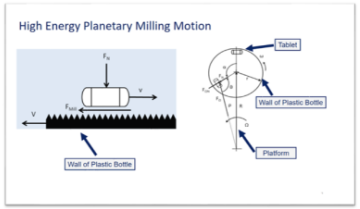

Figure 3: Mechanism of the wet milling process in the specialized plastic container

Figure 4: Compounding process for oral liquids using specialized plastic containers

Results & Discussion

- The compounded formulas possess a smooth texture and the required characteristics for proper dose withdrawal.
- The dose uniformity results were within 1% of the label claim. [Table 1]
- A beyond use date (BUD) of 1 month at room temperature was assigned to the compounded product. [Table 2 and Figure 5]
- The stability study results were within 5% of the label claim.

Table 1: Dose Uniformity Results for 20 µg/ml clonidine HCL suspension

Aliquot 1	20.2 (101% LC)
Aliquot 2	20.3 (102% LC)
Aliquot 3	20.0 (100% LC)
Average	20.2 (101% LC)
%RSD	0.84%

	20 mcg/mL Clonidine HCl 25C/60% RH (% Initial, %LC)
Initial	20.2 (101% LC)
1 Week	20.0 (99% I, 100% LC)
2 Week	19.9 (99% I, 100% LC)
3 Week	21.2 (105% I, 106% LC)
4 Week	20.9 (103% I, 105% LC)

Table 2: Stability data for 20 µg/ml clonidine HCl suspension

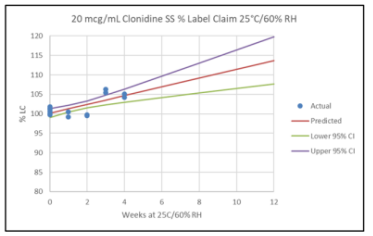

Figure 6: Stability data for 20 µg/ml clonidine HCl suspension

Conclusions

- The data demonstrate the effectiveness of the self-contained wet-milling technology to compound low-concentration homogenous suspensions that contain the entire dose.
- The wet-milling process results in excellent dose uniformity.
- Automation eliminates the variability introduced by manual procedures.
- The employment of a single-use disposable container for compounding, storage, and administration eliminates the need for cleaning and the risk of cross contamination.
- Use of a fully-enclosed compounding environment with added safeguards eliminates the potential exposure of personnel to aerosolized powders.

Disclosures

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.

- Joe B. D'Silva: Chief Scientific Officer and CEO, P&C Pharma
- William L. Boyko: Consultant Pharmacist, P&C Pharma
- Edmund J. Elder: Member of the 2015-2020 USP Compounding Expert Committee
- Michael Pugacz: Nothing to disclose
- Tina M. Wise: Nothing to disclose

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