Establishing a Beyond Use Date for Compounded Haloperidol Oral Suspension Prepared from Tablets Using a Novel Automated Wet-Milling Technology

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Introduction

Compounding of oral liquids from tablets and capsules is commonly conducted using a mortar and pestle to grind the solids into particles of an appropriate size.

A novel automated wet-milling technology was invented to enable compounding to be performed within a single-use multipurpose specialized plastic container. [Figure 1]

The container compounds, stores and dispenses the compounded product with no required product transfers. [Figure 2]

All of the compounding is undertaken within an enclosed environment. [Figure 3]

A study was undertaken using haloperidol tablets to demonstrate the efficiency of the process, the physical-chemical and microbiological quality and personalization of the compounded formulations, and the resultant benefits accrued to pharmacists and patients.

Methods

Haloperidol tablets were compounded into 1 and 5 mg/ml oral suspension preparations.

The requisite number of tablets and specified quantity of water were placed into the specialized plastic containers.

The containers are capped and placed inside the sealed holders within the milling unit. [Figure 3]

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 4]

A solid mixture of viscosity enhancers, flavors, sweeteners, buffers and preservatives was added to the suspension to produce a pharmaceutically acceptable oral liquid formula. [Figure 2]

Following compounding, the container serves the roles of storage and dispensing of the compounded product.

Several flavor options have been developed for personalization of the compounded formulas.

- A special high aroma formula, designated as Bananas Foster, was developed for patients with dementia.

Dose uniformity and chemical stability studies were undertaken using HPLC methods.

An antimicrobial effectiveness test was conducted per USP <51>

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: Compounding process for oral liquids using specialized plastic containers

Figure 3: Milling unit closed and opened showing containers in place

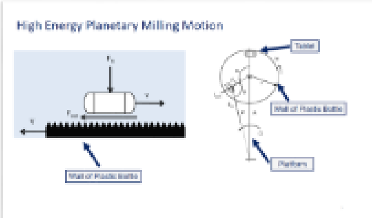

Figure 4: Mechanism of the wet milling process in the specialized plastic container

Results & Discussion

- The compounded formulas were found to have a smooth texture and the required characteristics for proper dose withdrawal.
- A beyond use date (BUD) of 1 month at room temperature was assigned to the compounded product. [Figures 5 and 6]
- The dose uniformity results were within 3% of the label claim. [Table 1]
- The stability study results were within 10% of the label claim.
- The compounded formulas satisfied the criteria specified in USP <51> Antimicrobial Effectiveness Testing.

Table 1: Dose Uniformity Results for Bananas Foster Suspensions

	1 mg/mL	5 mg/mL
Aliquot 1	1.01 (101% LC)	4.88 (98% LC)
Aliquot 2	1.02 (102% LC)	5.11 (102% LC)
Aliquot 3	1.01 (101% LC)	5.13 (103% LC)
Average	1.01 (101% LC)	5.04 (101% LC)
%RSD	0.39 %	2.80 %

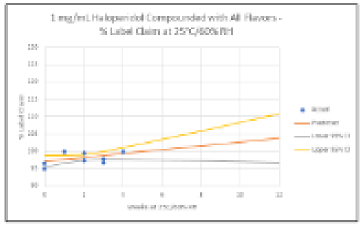

Figure 5: Stability data for 1 mg/ml Haloperidol Compounded Formula

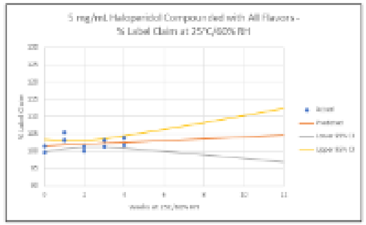

Figure 6: Stability data for 5 mg/ml Haloperidol Compounded Formula

Conclusions

- The data demonstrate the effectiveness of the novel wet-milling technology to compound homogenous suspensions.
- 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 greatly reduces the potential exposure of personnel to aerosolized powders.
- The novel wet-milling technology allows for the easy personalization of the compounded formulas with respect to drug concentration, flavors and viscosity.

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 Innovation Officer and CEO, P&C Pharma
- Karen J. Jones: Nothing to disclose
- John C. Walton: Nothing to disclose
- Annie C. Schuelke: Nothing to disclose
- Edmund J. Elder: Member of the 2015-2020 USP Compounding Expert Committee

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