Physicochemical and Microbiological Stability of Melatonin 5 mg/mL Oral Compounded Suspension

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BACKGROUND:

Melatonin is a pineal hormone commonly prescribed to children (2 mg/mL or 5 mg/mL) to treat insomnia (sleep onset and delayed sleep phase syndrome), although it is not licensed for these indications. In most countries, including Australia, there is no melatonin oral liquid commercially available. Therefore, there is a clinical need for an extemporaneous preparation of melatonin adapted to children.

PURPOSE:

To develop and test a melatonin oral compounded suspension with an extended beyond-use-date (BUD) for use particularly in pediatric patients.

METHOD:

A batch of 1,000 mL (Lot #: 111220-RT) was prepared for melatonin 5 mg/mL oral compounded suspension by adding the active ingredient to SuspendIt, a proprietary oral vehicle, as well as the following excipients: Steviol Glycosides 95% 0.2 g, Citric Acid USP Monohydrate (powder) 0.935 g, Sodium Citrate USP Anhydrous 1.432 g and flavor (marshmallow, artificial) 0.5 mL. The oral compounded suspension was evenly distributed into six prescription oval amber plastic bottles and stored for 180 days in an environmentally controlled chamber at a temperature of $25^0C \pm 2^0C$ and relative humidity of 60% ± 5%. At pre-determined time points [0, 14, 30, 60, 90 and 180 days], a study sample (one unopened bottle) was withdrawn from the storage condition, shaken vigorously and tested for physicochemical and microbiological stability. The physical characterization consisted of observing all samples for appearance/color and testing for pH (Horiba LaquaTwin pH meter). The chemical characterization consisted of assay testing employing a stability-indicating High Performance Liquid Chromatography (HPLC) method (Waters Acquity) developed and validated by Eagle Analytical Laboratories (Texas, US). The microbiological stability followed the United States Pharmacopoeia (USP) Chapter <51> Anti-Microbial Effectiveness (AME) testing method.

RESULTS:

- Considering the physical characterization, the melatonin oral compounded suspension exhibited a homogeneous white to light beige colour and a smooth appearance. The range of pH (4.58-4.72) was within the acceptable limits.
- Considering the chemical characterization, the chromatographic assay method was validated by evaluating the system specificity, linearity and range, accuracy/recovery, precision (repeatability and intermediate), solution stability, robustness, and suitability.
- The percent potency was calculated taking into account the baseline measurements on day 0. The potency of the melatonin suspension remained within ±10% of the specifications throughout the study, as follows: 98%-107%.
- The preservative system in SuspendIt successfully protected the oral compounded suspensions from microbial contamination since there was no growth of challenge microorganisms throughout the study for all samples.

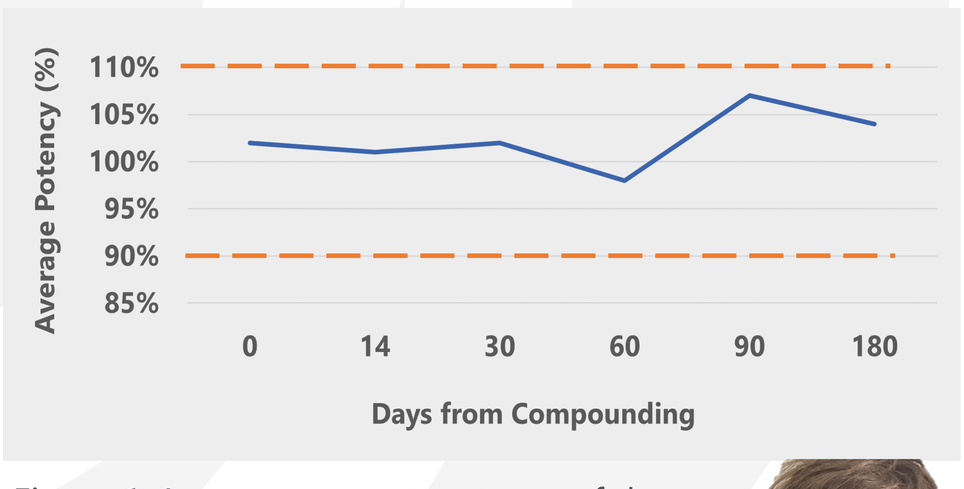

Figure 1. Average percent potency of the melatonin 5 mg/mL oral compounded suspension over 6 months from compounding (extemporaneous preparation). Dashed lines represent the lower and upper limits, corresponding to 90% and 110% of the labelled concentration, respectively.

CONCLUSION:

Oral compounded suspensions are rapidly prepared, allow dosing flexibility and are easy to administer. However, community and hospital pharmacists need validated stability studies to prepare oral liquids with quality and safety. A palatable, sugar-free formula was developed for melatonin 5 mg/mL in SuspendIt to facilitate the extemporaneous preparation in the community setting. The corresponding BUD was determined using a valid, stability-indicating analytical method and it was concluded that the melatonin 5 mg/mL oral compounded suspension is physically, chemically and microbiologically stable in SuspendIt at room temperature for up to 180 days.