Physicochemical and Microbiological Stability of Compounded Rifaximin Oral Suspensions in PCCA Base, SuspendIt®

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BACKGROUND

Rifaximin is a rifamycin-derived broad-spectrum antibiotic with activity against gram-positive, gram-negative, aerobic, and anaerobic bacteria. In the United States, rifaximin is manufactured solely as an oral tablet, which limits dosage options and is not suitable for persons who have difficulty swallowing. A review of the therapeutic uses of rifaximin reveals the need for flexibility in dosing. This flexibility is readily achieved using an oral liquid dosage form. However, no manufactured liquid dosage form of rifaximin currently exists. An extemporaneously compounded suspension from commercial tablets would provide a flexible, customizable option to meet unique patient needs with convenient and accurate dosing options for pediatric and adult patients.

PURPOSE

To determine the physicochemical and microbiological stability of extemporaneously compounded rifaximin suspensions using commercially available tablets in the proprietary oral vehicle PCCA Base, SuspendIt, a sugar-free, paraben-free, dye-free and gluten-free thixotropic suspending agent containing a natural sweetener obtained from the monk fruit. It thickens upon standing to minimize settling of any insoluble drug particles, and becomes fluid upon shaking to allow convenient pouring during administration to the patient.

METHODS

Suspensions of rifaximin were prepared from commercially available Xifaxan® 550 mg tablets in PCCA SuspendIt at 20-mg/mL and 40-mg/mL concentrations, to represent a range in which the drug is commonly dosed. Samples were stored in plastic amber prescription bottles at room temperature (25^{0}C). Samples were assayed initially, and at pre-determined time intervals (14, 30, 60, 90 and 180 days) over a 6-month period. The chemical characterization employed a stability-indicating Ultra High Performance Liquid Chromatography (UPLC) assay method (Waters Acquity) developed and validated by Eagle Analytical Laboratories (Texas, USA). Physical data such as pH and appearance were noted. Samples were also tested for microbiological stability in compliance with the United States Pharmacopoeia (USP) Chapter <51> Anti-Microbial Effectiveness (AME) testing method.

RESULTS

- Rifaximin tablets formed a homogeneous yellowish-orange suspension in PCCA SuspendIt. The pH range (5.10-5.33) for both drug concentrations displayed no significant changes over the test period.
- The UPLC assay method was validated by evaluating the system specificity, linearity and range, accuracy and recovery, precision (repeatability and intermediate), solution stability, robustness, and suitability.
- Drug concentrations were calculated in mg/mL and also as a percentage based on the initial measurements on day 0. The concentrations of the rifaximin suspensions remained within ±10% of the USP specifications (93-106%) throughout the study (Tables 1 & 2).
- The antimicrobial preservative system in SuspendIt successfully protected the oral compounded suspensions from microbial contamination by preventing growth of challenge microorganisms throughout the study for all samples.

Table 1. Rifaximin Concentration (mg/mL) in PCCA SuspendIt

Time	20-mg/mL	40-mg/mL
	Xifaxan® Tablets	Xifaxan® Tablets
Day 0	20.1	41.4
Day 14	19.9	41.1
Day 30	20.6	42.6
Day 60	20.6	41.8
Day 90	19.7	40.1
Day 180	18.9	38.6

Table 2. Percent of Rifaximin in PCCA SuspendIt Relative to the labeled concentration

Time	20-mg/mL	40-mg/mL
	Xifaxan® Tablets	Xifaxan® Tablets
Day 0	101	104
Day 14	99.5	103
Day 30	103	107
Day 60	103	105
Day 90	98.5	100.3
Day 180	94.5	96.5

CONCLUSION

A robust stability indicating UPLC assay method for the determination of rifaximin in PCCA SuspendIt was used to determine the chemical stability of the 20-mg/mL and 40-mg/mL concentrations of Rifaximin tablets in PCCA SuspendIt at 25^{0}C. This study demonstrated that rifaximin suspensions in PCCA SuspendIt are physically, chemically and microbiologically stable at room temperature at both concentrations studied for up to 180 days, thus providing a viable, compounded alternative for rifaximin in a liquid dosage form with an extended beyond-use-date to meet patient needs.