Microbiological Stability Testing of Extemporaneously Compounded Omeprazole 2 mg/mL in Oral Mix™ Dry Alka, SF Cherry Flavored and Unflavored

Introduction

In response to the need for a suitable oral liquid preparation with improved palatability and stability for acid-labile APIs such as proton-pump inhibitors (PPIs), MEDISCA introduced Oral Mix Dry Alka, SF. This uniform powder for reconstitution is formulated to quickly and easily compound APIs that require an alkaline medium, such as omeprazole, into highly palatable oral suspensions. MEDISCA's Oral Mix Dry Alka, SF provides an alternative that is free of sugar, preservatives and dyes, which is often required when administering medication to critical groups such as geriatric and pediatric patients who cannot swallow commercial tablets. Available in cherry and unflavored options, these vehicles allow for further customization based on patient preference.

The chemical and physical stability of extemporaneously compounded Omeprazole 2, 5 and 10 mg/mL in Oral Mix Dry Alka, SF (Cherry Flavored) was previously studied and proven for up to 70 days in refrigerated conditions using validated stability-indicating methods[1]. Although preservatives can be problematic in certain patient groups, they typically serve a crucial function in ensuring that an aqueous preparation remains free from microbial growth. When a preservative-free vehicle is required, the healthcare provider must be aware that the preparation will be more susceptible to contamination. Given the preservative-free nature of Oral Mix Dry Alka, SF and the vulnerable nature of the pediatric and geriatric patient population, microbiological testing was deemed necessary to evaluate the overall safety and stability of the compounded preparation.

Objective

The objective of this study was to demonstrate the bioburden of extemporaneously compounded omeprazole suspension 2 mg/mL in MEDISCA's Oral Mix Dry Alka, SF Cherry Flavored and Unflavored through total aerobic microbial count (TAMC), total combined yeast and molds count (TYMC) and Escherichia Coli testing at multiple time points for a duration of 70 days.

Methods

Triplicate batches of omeprazole suspensions (2 mg/mL) were prepared using pre-weighed Oral Mix Dry Alka, SF (Cherry Flavored) powder (6.35 g; MEDISCA Pharmaceutique Inc, Montreal, Quebec; lot R36123A) and Oral Mix Dry Alka, SF (Unflavored) powder (6.35 g; MEDISCA Pharmaceutique Inc, Montreal, Quebec; lot R36123) in 100 mL amber polypropylene (PP) UV-Resistant (low actinic) bottles (MEDISCA Pharmaceutique Inc, Montreal, Quebec; product no. 6347). Omeprazole USP (200 mg; MEDISCA Pharmaceutique Inc, Montreal Quebec; lot 615172) was mixed into the pre-weighed base, followed by approximately 60 mL of purified water, USP (MEDISCA Pharmaceutique Inc, Montreal, Quebec; lot 617843). The suspension was shaken vigorously by hand for no less than 60 seconds until uniform. Additional water was added to achieve the final volume of the graduated 100 mL PP bottle and then shaken to form a uniform suspension. A press-in bottle adapter (33 mm) was then inserted and the bottles were stored at 4 °C with the use of a temperature-controlled refrigerator for up to 70 days.

During testing, the samples for all 8 time points were drawn from the same bottle using the press-in bottle adaptor. The use of the press-in bottle adaptor significantly decreases the bottle opening and in turn minimizes exposure of the compounded preparation, which is ideal for unpreserved preparations.

Moreover, as the base is preservative-free, USP <51> Antimicrobial Effectiveness Testing was not performed and alternatively, microbiological stability was assessed through TAMC, TYMC and detection of E. Coli testing. Testing was conducted using a rapid microbiological method that has been validated as equivalent to USP <61> and USP <62> with acceptance criteria set by USP <1111>. This procedure uses an optical instrument system (BioLumix; Neogen Corporation, Lansing, Michigan) that detects microorganisms based on a function of color or fluorescence. Samples are diluted according to the specification in test vials with defined growth media, and detection is recorded during a 30 hour, 35°C incubation period for TAMC, and a 48 hour, 28°C incubation period for TYMC. Suitability testing was carried out on the compounded preparations to ensure that microbial activity can be detected using this procedure (Procedure M500; CED Analytical Labs, Irving, Texas).

Results

On each testing day, TAMC and TYMC values met the acceptance criteria and there was no presence of E. Coli for all samples as seen in Table 1 and Table 2. The results were validated, as testing was performed on three different batches for each vehicle. Both Cherry and Unflavored suspensions remained microbiologically stable throughout the entire 70-day testing period.

Table 1. Microbiological testing results for Oral Mix Dry Alka, SF (Cherry Flavored)

	Test	Acceptance Criteria	Day 0	Day 7	Day 14	Day 21	Day 28	Day 42	Day 56	Day 70
BATCH 1	Description	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid
	TAMC	≤100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g
	TYMC	≤10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g
	E.Coli	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
BATCH 2	Description	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid
	TAMC	≤100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g
	TYMC	≤10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g
	E.Coli	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
BATCH 3	Description	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid
	TAMC	≤100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g
	TYMC	≤10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g
	E.Coli	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent

TAMC: Total Aerobic and Microbial Count TYMC: Total Combined Yeast & Molds Count

Table 2. Microbiological testing results for Oral Mix Dry Alka, SF (Unflavored)

	Test	Acceptance Criteria	Day 0	Day 7	Day 14	Day 21	Day 28	Day 42	Day 56	Day 70
BATCH 1	Description	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid
	TAMC	≤100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g
	TYMC	≤10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g
	E.Coli	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
BATCH 2	Description	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid
	TAMC	≤100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g
	TYMC	≤10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g
	E.Coli	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
BATCH 3	Description	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid	Milky Liquid
	TAMC	≤100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g	<100 cfu/g
	TYMC	≤10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g	<10 cfu/g
	E.Coli	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent

TAMC: Total Aerobic and Microbial Count TYMC: Total Combined Yeast & Molds Count

Conclusion

As aqueous pharmaceutical products provide an ideal environment for microbial growth, good compounding practices along with the use of preventative measures, such as the use of press-in bottle adaptors, must be followed when administering non-preserved compounded preparations to patients. With validated microbiological stability of up to 70 days, Oral Mix Dry Alka, SF Cherry Flavored and Unflavored are ideal suspending vehicles for compounded omeprazole 2 mg/mL preparations.

1. Stability of Extemporaneously Compounded Omeprazole 2, 5 and 10 mg/mL in Oral Mix Dry Alka, SF (Cherry Flavored) (2017)