

Physicochemical stability of omeprazole 2 mg/mL and 10 mg/mL oral suspensions in SuspendIt®

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Omeprazole is a proton pump inhibitor commonly used in children for the short-term treatment of gastro-oesophageal reflux disease and gastric/duodenal ulcers. The commercially available capsules and tablets are not licensed for use in children and do not permit age/weight adjustments of the dosage strength¹. As such, an alternative extemporaneous preparation was developed for omeprazole 2 mg/mL and 10 mg/mL in the child-appropriate vehicle SuspendIt®. The

Methodology



corresponding Beyond-Use Dates (BUDs) were determined by testing the physicochemical stability of the oral suspensions.

A batch of 1,000 mL was prepared for omeprazole 2 mg/mL and for omeprazole 10 mg/mL by adding the active ingredient to SuspendIt®, as well as the following excipients: acesulfame potassium and steviol glycosides 95% 3 g, sodium bicarbonate 110 g, flavor (banana), and sodium hydroxide 10% (as required, pH adjustment), as displayed in Table 1. Each oral suspension was distributed into 50-mL amber plastic bottles and the study samples were then stored for 182 days in a laboratory refrigerator at a temperature of 5°C ± 3°C; and in an environmentally controlled chamber at a temperature of 25°C ± 2°C and relative humidity of 60% ± 5%. The physical characterization consisted in observing all samples for appearance/color and odor, and testing for pH (Horiba LaquaTwin pH meter) and density (Fisher Scientific grease pycnometer). The chemical characterization consisted in a validated, stability-indicating Ultra-High Performance Liquid Chromatography (UHPLC) assay testing (Waters Acquity). At pre-determined time points [0 (baseline), 7, 14, 28, 42, 63, 90, 119, and 182 days], a study sample (one unopened bottle) of each strength was withdrawn from the storage conditions, shaken vigorously and tested for physicochemical stability.

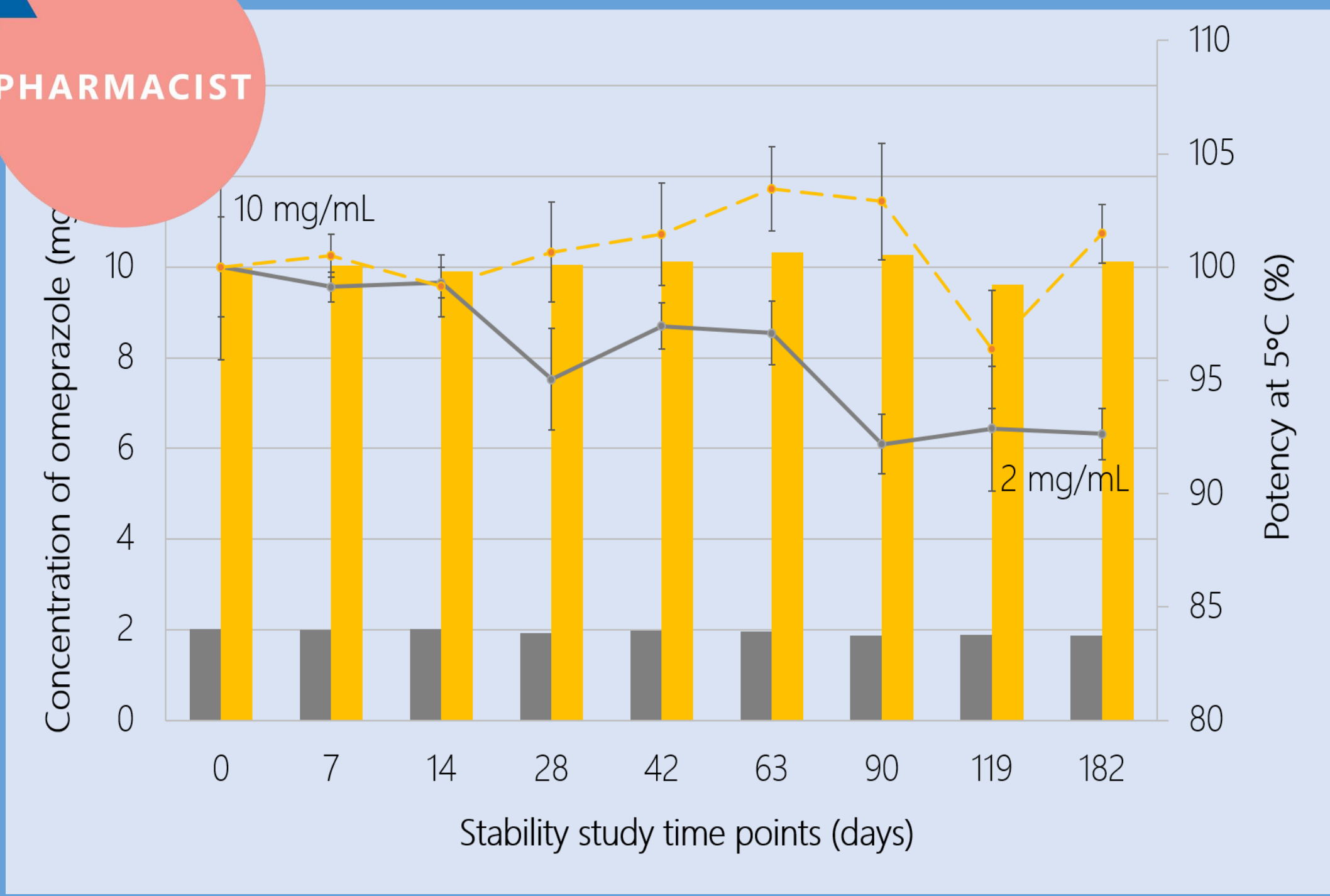


Rx	
Omeprazole	0.2 or 1 g
Acesulfame potassium	0.3 g
Steviol glycosides 95%	0.3 g
Sodium bicarbonate	11 g
Flavor (Banana)	qs
Sodium hydroxide 10%	qs
Vehicle: SuspendIt®	qs 100 mL

Results & Discussion



Considering the physical characterization, the omeprazole oral suspensions stored at refrigerated temperature exhibited a homogeneous yellow color, opaque appearance and a banana odor throughout the study. The range of densities (1.066-1.080 g/mL for 2 mg/mL and 1.068-1.078 g/mL for 10 mg/mL) and the range of pH (7.92-8.84 for 2 mg/mL and 8.00-8.85 for 10 mg/mL) were within the limits. The omeprazole oral suspensions stored at room temperature, on the other hand, exhibited remarkable changes of color, appearance and odor over the 182 days of the study. The range of densities and pH though were within the limits: 1.074-1.083 g/mL and 8.05-8.85 for 2 mg/mL; 1.069-1.090 g/mL and 8.12-8.86 for 10 mg/mL.



Considering the chemical characterization, the chromatographic assay method was validated by evaluating the system suitability, linearity, accuracy, precision (repeatability and intermediate), robustness, solution stability, and specificity. Subsequently, the percent potency was calculated taking into account the baseline measurements on day 0. The potency of the oral suspensions remained within the ±10% specifications² throughout the study for the refrigerated temperature only: 92.19% - 99.30% for 2 mg/mL and 96.37% - 103.45% for 10 mg/mL. For the room temperature, the potency was below the limits from day 14 (2 mg/mL) and day 63 (10 mg/mL). As a result, the omeprazole oral suspensions from 2 mg/mL up to 10 mg/mL (bracketed study) are physically and chemically stable at 5°C (only), for 182 days in amber plastic bottles.

The BUD of the omeprazole 2 mg/mL - 10 mg/mL oral suspensions (SuspendIt®) is 6 months at refrigerated temperature, in amber plastic bottles.

1. Paediatric Formulary Committee (2016) BNF for Children. London: BMJ Group and Pharmaceutical Press, p.51,54-5.
2. The United States Pharmacopeial Convention (2016c) 'General Requirements / <2> Oral Drug Products – Product Quality Tests'. USP 39 – NF 34. Rockville: USP, p.77.

