Physicochemical Stability of Allopurinol, Amitriptyline Hydrochloride, Amlodipine Besylate, Clindamycin Hydrochloride, Hydrocortisone, Metronidazole, Naltrexone Hydrochloride, Spironolactone, Trimethoprim with Sulfadiazine, and Ursodiol Extemporaneously Compounded Oral Suspensions in PCCA Base, SuspendIt

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Background

Extemporaneously compounded oral suspensions are commonly prepared to meet the individual needs of pediatric and geriatric patients. However, their formulation and stability are usually complex.

The purpose of these studies was to determine the physicochemical stability and, when applicable, the microbiological stability of 10 extemporaneously compounded oral suspensions in the PCCA Base, SuspendIt. This base is a sugar-free, paraben-free, dye-free, and gluten-free thixotropic vehicle 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.

Aims

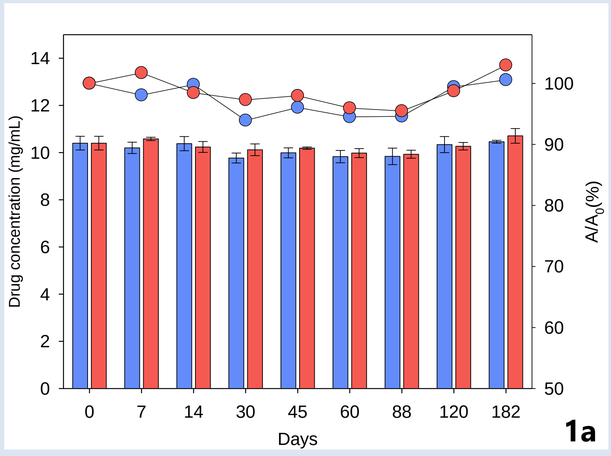
Ten physicochemical stability studies were undertaken to determine the beyond-use-dates (BUDs) of the following oral suspensions: allopurinol 10 and 20 mg/mL; amitriptyline hydrochloride 1 and 5 mg/mL; amlodipine besylate 0.5 and 10 mg/mL; clindamycin hydrochloride 10 mg/mL; hydrocortisone 1 and 20 mg/mL; metronidazole 25 and 50 mg/mL; naltrexone hydrochloride 0.5 and 5 mg/mL; spironolactone 5 mg/mL; trimethoprim 20 mg/mL with sulfadiazine 100 mg/mL; and ursodiol 50 and 100 mg/mL. Microbiological stability studies were also undertaken for amitriptyline, hydrocortisone and metronidazole. The study design included two concentrations for most active substances to provide stability documentation over a bracketed range for eventual use by compounding pharmacists.

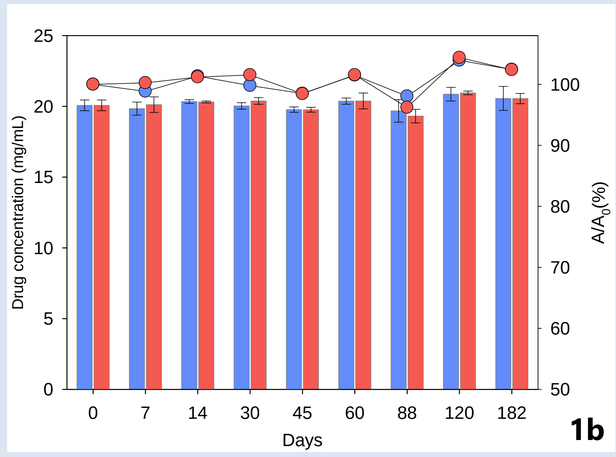
Methods

Samples were prepared and stored in plastic amber prescription bottles at two temperatures (5°C and 25°C) for the allopurinol, amitriptyline, amlodipine, hydrocortisone, metronidazole, naltrexone and ursodiol oral suspensions; and three temperatures (5°C, 25°C and 40°C) for the clindamycin, spironolactone, and trimethoprim with sulfadiazine oral suspensions. Chemical stability was tested and validated using high-performance liquid chromatographic (HPLC) assay at baseline, and subsequently at eight pre-determined time-points (e.g. 7, 14, 30, 45, 60, 91, 120 and 182 days). The physical stability was tested by monitoring the pH, viscosity and appearance of the suspensions over a period of six months. The microbiological stability was tested by evaluating the growth of challenge microorganisms per the USP Chapter <51> AME Test.

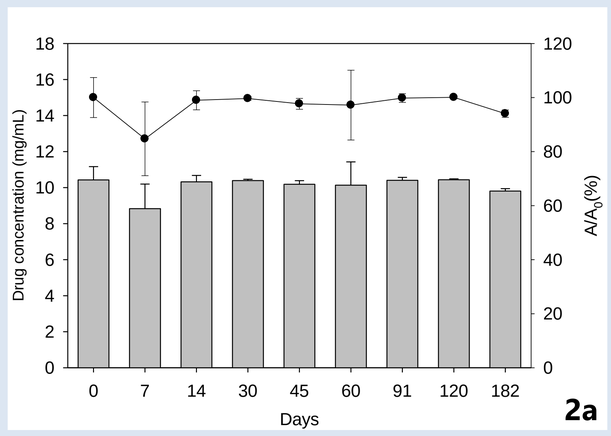
Results

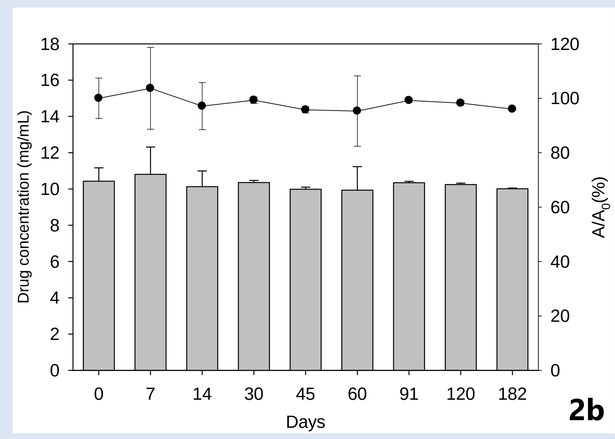
Most of the extemporaneously compounded oral suspensions retained at least 90% of the initial concentration (label claim) and underwent no significant physical or microbiological changes for the study period of 6 months. Only amlodipine besylate 0.5 and 10 mg/mL was stable for a shorter period of time (90 days in the refrigerator and 7 days at room temperature). Figures 1-3 display the changes observed in the concentrations for selected active substances (allopurinol, clindamycin, sulfadiazine and trimethoprim), at different storage temperatures. As observed, the drug concentrations stayed above 90% which demonstrates the chemical stability of these active substances.



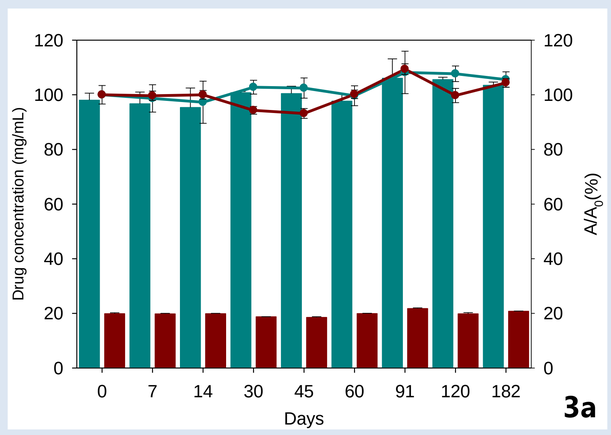


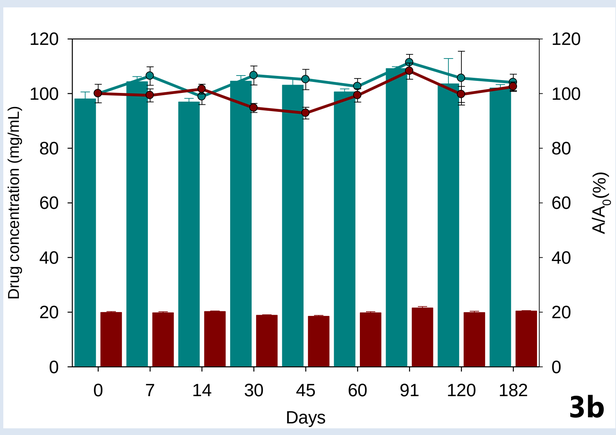
Figures 1a and 1b. *Change in drug concentration over 182 days on left axis for the 10 mg/mL (1a) and 20 mg/mL (1b) samples of Allopurinol in SuspendIt™ stored at 5°C (blue) and 25°C (red); and relative change in percent on right axis as compared to initial concentration [A/Ao = drug content at time t (A) over initial drug content (Ao) x100].*





Figures 2a and 2b. *Change in drug concentration over 182 days for Clindamycin in SuspendIt™ stored at 5°C (2a) and 25°C (2b); and relative change in percent as compared to initial concentration (At/Ao = drug content at time t (At) over initial drug content (Ao) x100).*





Figures 3a and 3b. *Change in drug concentration over 182 days for Sulfadiazine (teal) and Trimethoprim (maroon) in SuspendIt™ stored at 5°C (3a) and 25°C (3b); and relative change in percent as compared to initial concentration (At/Ao = drug content at time t (At) over initial drug content (Ao) x100).*

Summary/Conclusion

A robust stability-indicating HPLC assay method was developed, validated, and used to determine the chemical stability of 11 active substances in PCCA Base, SuspendIt at 5°C and 25°C. The physical stability and, when applicable, the microbiological stability were also determined. An extended beyond-use-date of six months may be assigned to the allopurinol, amitriptyline, clindamycin, hydrocortisone, metronidazole, naltrexone, spironolactone, trimethoprim with sulfadiazine, and ursodiol oral suspensions in PCCA Base, SuspendIt when stored in the refrigerator or at room temperature. The amlodipine oral suspension should be stored in the refrigerator for a beyond-use-date of 3 months.

Acknowledgement

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