Validated Stability Studies for 40 Paediatric Extemporaneously Compounded Oral Solutions and Suspensions (SuspendIt®)

Maria Carvalho, Melissa Merrell Rhoads, Courtaney Davis, Kendice Ip, August S. Bassani, A.J. Day and Daniel Banov

Professional Compounding Centers of America (PCCA), Texas, USA

PCCAScience@pccarx.com

fip SEVILLE 2022 FIP WORLD CONGRESS 18-22 September

BACKGROUND:

The pharmacological treatment of children is often challenging because most of the commercial medications are solid dosage forms (tablets and capsules) indicated for adults. There is a general lack of age-appropriate formulations, and the extemporaneous preparation of compounded oral liquids represents a key therapeutic alternative for the paediatric population.

INTRODUCTION:

Oral solutions and suspensions may be rapidly prepared, allow dosing flexibility and are easy to administer. However, hospital pharmacists need standard operating procedures and validated stability studies to compound with assured quality and safety. A total of 40 paediatric oral liquids commonly prescribed for children were extemporaneously compounded by adding the active substance(s) and, when applicable, additional excipients (e.g. flavors and sweeteners) to the sugar-free, paraben-free and gluten-free vehicle SuspendIt. The standardised concentrations were based on the 'Standardize 4 Safety' initiative by the ASHP, as follows: acetazolamide 25 mg/mL, amphotericin B 100 mg/mL, atenolol 2 mg/mL, baclofen 5-10 mg/mL, budesonide 0.1-4 mg/mL, buspirone hydrochloride 2.5 mg/mL, captopril 1-5 mg/mL, clonazepam 0.1 mg/mL, dipyridamole 10 mg/mL, fluconazole 50 mg/mL, fluoxetine 1-10 mg/mL, gabapentin 25-100 mg/mL, hydrochlorothiazide 5-10 mg/mL, hydroxychloroquine sulphate 25 mg/mL, hydroxyurea 100 mg/mL, ketoconazole 20 mg/mL, lamotrigine 1 mg/mL, lansoprazole 3-10 mg/mL, melatonin 5 mg/mL, metoprolol tartrate 1-10 mg/mL, mexiletine hydrochloride 10 mg/mL, nadolol 10 mg/mL, omeprazole 2-10 mg/mL, pantoprazole 2 mg/mL, phenobarbital 1-50 mg/mL, phytonadione 1 mg/mL, prednisolone 1-10 mg/mL, propylthiouracil 5 mg/mL, pyridoxine hydrochloride 1 mg/mL, sildenafil 2.5 mg/mL, spironolactone 5 mg/mL and hydrochlorothiazide 5 mg/mL, sulfasalazine 100 mg/mL, terbutaline sulphate 1 mg/mL, theophylline 25-100 mg/mL, thiamine hydrochloride 25 mg/mL, topiramate 5-25 mg/mL, tramadol hydrochloride 5 mg/mL, trazodone hydrochloride 10 mg/mL, verapamil hydrochloride 50 mg/mL and zonisamide 10-50 mg/mL.

The corresponding Beyond-Use Dates (BUD) were determined by testing the physicochemical stability of the oral liquids at one or two temperatures (5°C and/or 25°C).

METHOD:

The physical characterization consisted of observing all samples for appearance/colour and testing for pH. The chemical characterization consisted of assay testing employing a stability-indicating Ultra-High Performance Liquid Chromatography (UHPLC) method (Waters Acquity) developed and validated by Eagle Analytical Laboratories (Texas, USA) or Professional Compounding Centers of America (Texas, USA). Samples were tested at baseline and subsequently at pre-determined time-points for a total of 90 or 180 days.

Acetazolamide, amphotericin B, atenolol, baclofen, budesonide, buspirone, captopril, clonazepam, dipyridamole, fluconazole, fluoxetine, gabapentin, hydrochlorothiazide, hydroxychloroquine sulphate, hydroxyurea, ketoconazole, lamotrigine, lansoprazole, melatonin, metoprolol tartrate, mexiletine hydrochloride, nadolol, omeprazole, pantoprazole, phenobarbital, phytonadione, prednisolone, propylthiouracil, pyridoxine hydrochloride, sildenafil, spironolactone and hydrochlorothiazide, sulfasalazine, terbutaline sulphate, theophylline, thiamine hydrochloride, topiramate, tramadol hydrochloride, trazodone hydrochloride, verapamil hydrochloride and zonisamide.

RESULTS:

- The BUD for acetazolamide, amphotericin B, atenolol, baclofen, budesonide, clonazepam, gabapentin, hydrochlorothiazide, hydroxychloroquine, hydroxyurea, metoprolol, prednisolone, theophylline, thiamine, topiramate, tramadol, trazodone, verapamil and zonisamide, in SuspendIt, is 6 months at room temperature only.
- The BUD for melatonin in SuspendIt is 3 months, at room temperature only.
- The BUD for fluconazole and phenobarbital in SuspendIt is 6 months at both refrigerator and room temperature.
- The BUD for buspirone, captopril, dipyridamole, fluoxetine, ketoconazole, lamotrigine, lansoprazole, mexiletine, nadolol, omeprazole, pantoprazole, phytonadione, propylthiouracil, pyridoxine, sildenafil, spironolactone and hydrochlorothiazide, sulfasalazine and terbutaline, in SuspendIt, is 6 months at refrigerator temperature only.

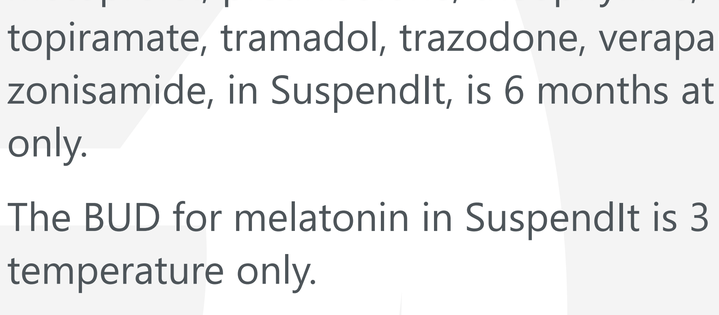

Figure 2. Chromatogram of the phenobarbital 50 mg/mL oral suspension stored at room temperature on day 182.

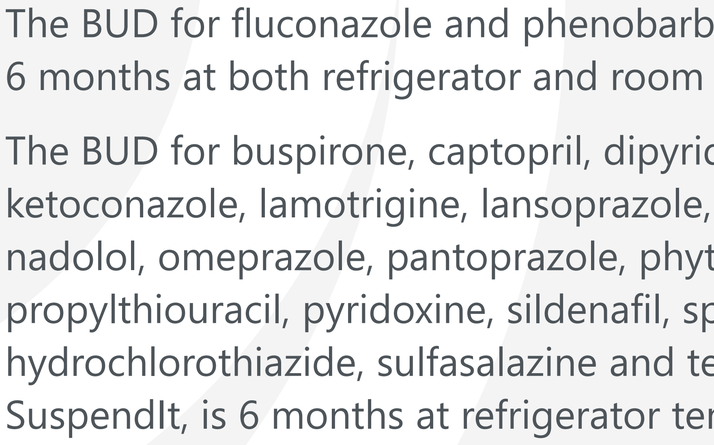

Figure 3. Concentration and percent potency of the lansoprazole oral suspensions 3 mg/mL (grey columns/line) and 10 mg/mL (yellow columns/line), stored at 5°C over 181 days.

CONCLUSION:

Standardised, palatable compounded oral liquids were developed and tested to facilitate the extemporaneous preparation in the hospital setting. It was concluded that all 40 active substances are physically and chemically stable in the vehicle SuspendIt for at least 90 days.