

STABILITY STUDY OF 100 MG/ML PAEDIATRIC PYRAZINAMIDE ORAL SUSPENSION IN SYRSPEND

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BACKGROUND

Pyrazinamide (PZA) is an antituberculosis agent used in adjunctive treatment of tuberculosis infection in combination with other antituberculosis agents as isoniazid, rifampicin and ethambutol. Tablet form is unsuitable for pediatric patients and leads the pharmacist to produce oral suspension. Data about PZA stability in oral suspension are scarce and were got several decades ago. Thus, new stability informations are needed.

PURPOSE

Determine the stability of 100 mg/mL PZA oral suspension in commercial compounding excipient : Syrspend® SF PH4.

MATERIAL AND METHODS

Stability study according to the ICH guidelines

3 batches of oral suspension of PZA at 100 mg/mL → storage at room temperature in amber vials 

Day : D0 → D3 → D5 → D8 → D15 → D30 → D60 → D90

Physical Stability



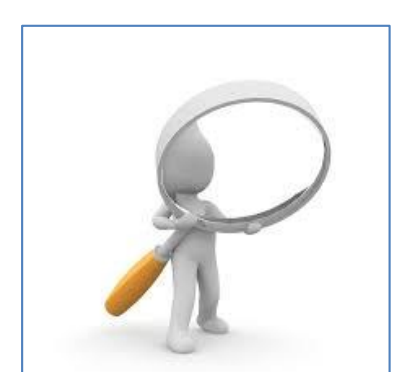
Mesure of pH

pHénoménal® VWR
pHmeter



Mesure of osmolality

Advanced Instruments
Model 3250®
Osmometer



Visual inspection

Chemical Stability



- Using a validated analytical method
- Quantification of PZA
- Detection of degradation product

- High Performance Liquid Chromatography with Ultraviolet detection
- Mobile phase : acetonitrile/phosphate buffer pH 3 (40:60 v/v)
- Column : WATERS C18 ATLANTIS T3 column (150 x 4.6 mm, 5 µm)
- Flow rate : 1 ml/min; λ=270 nm

Microbiological Stability

- Test using colony counts on media platings
- Trypticase Soja (35°C)
- 1/10e dilution of suspension in water

- D0
- D15
- D30
- D60
- D90



RESULTS

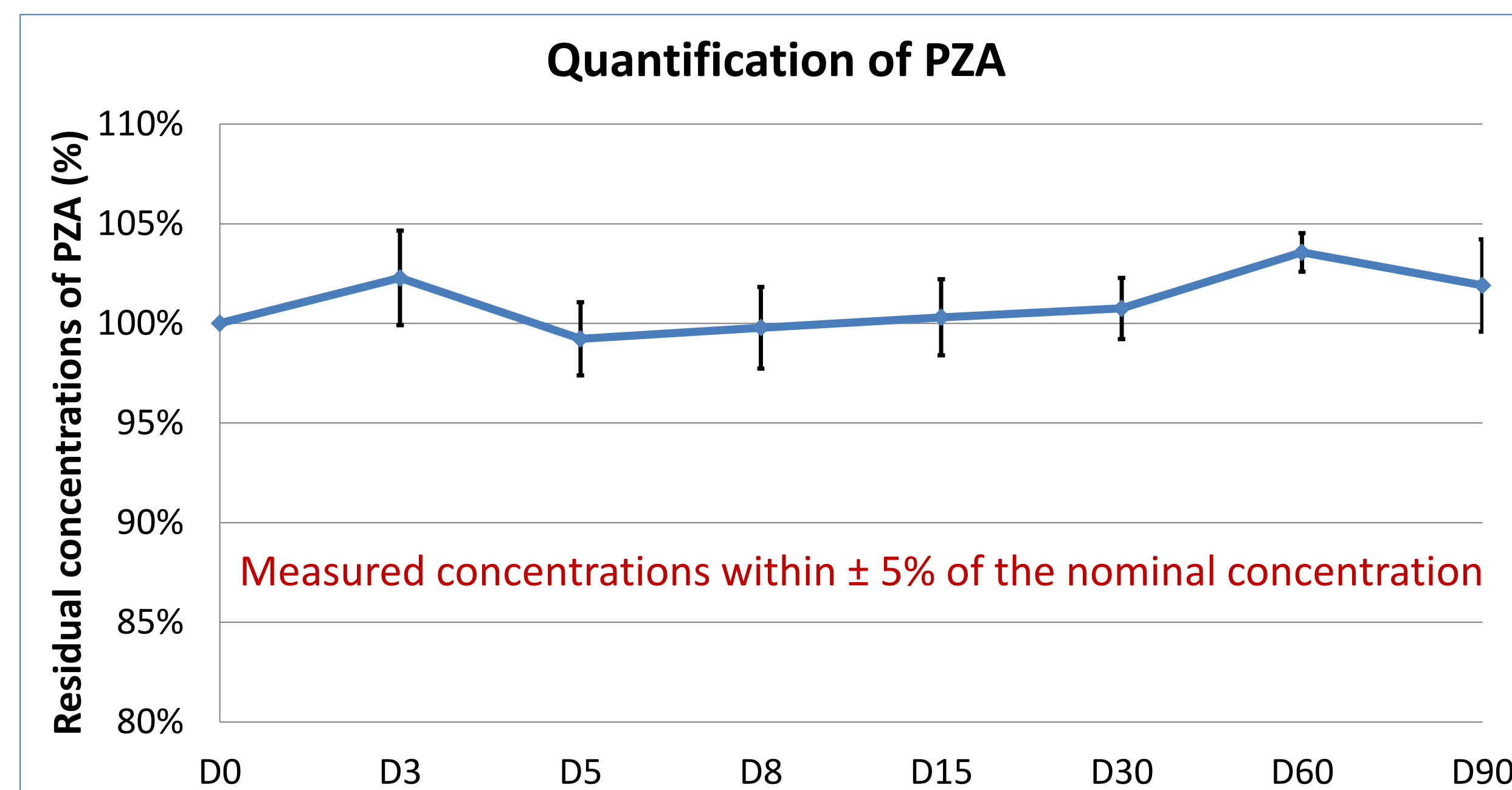
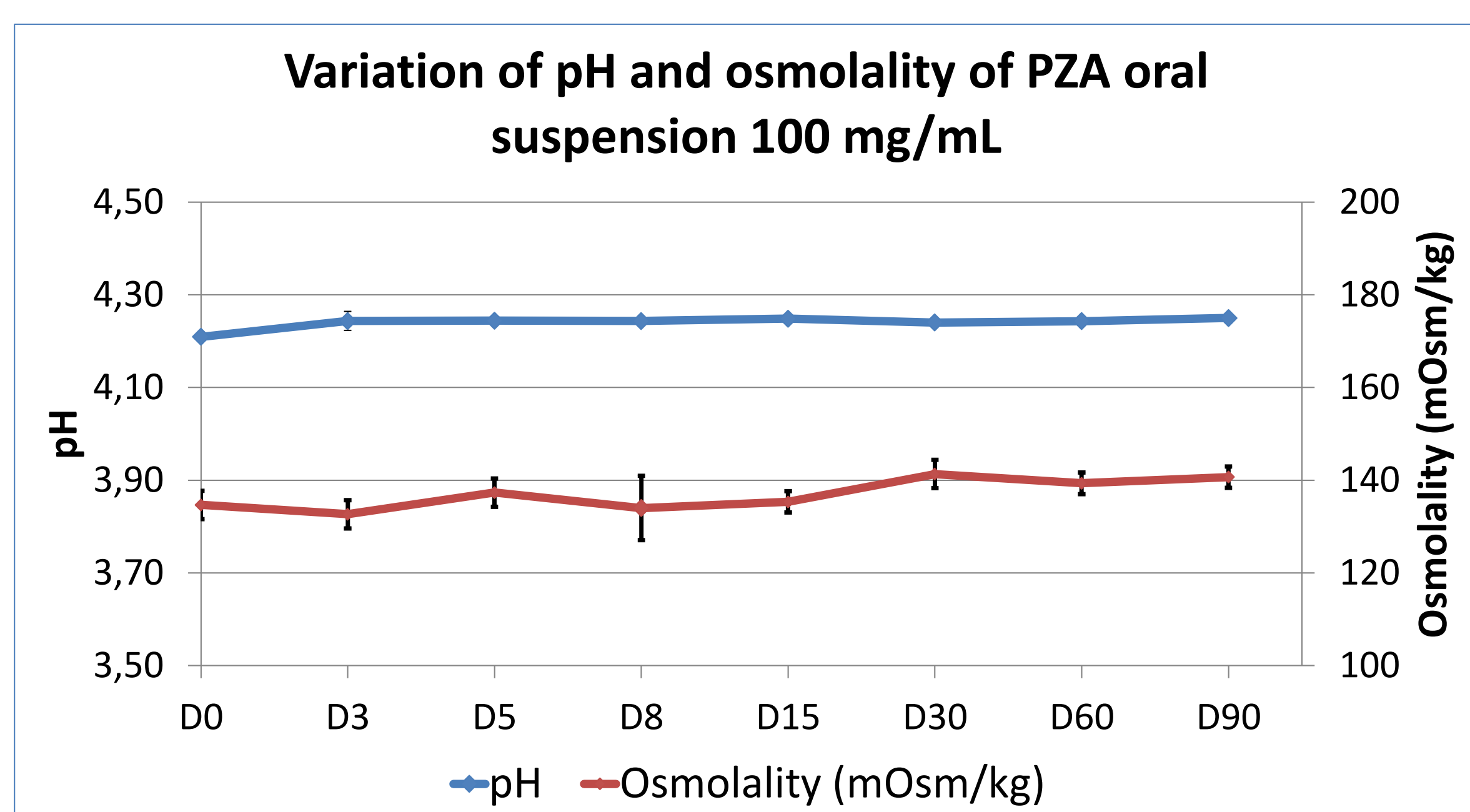
Physical stability

- ✓ No change of physical properties was observed during the studied period

Microbiological stability

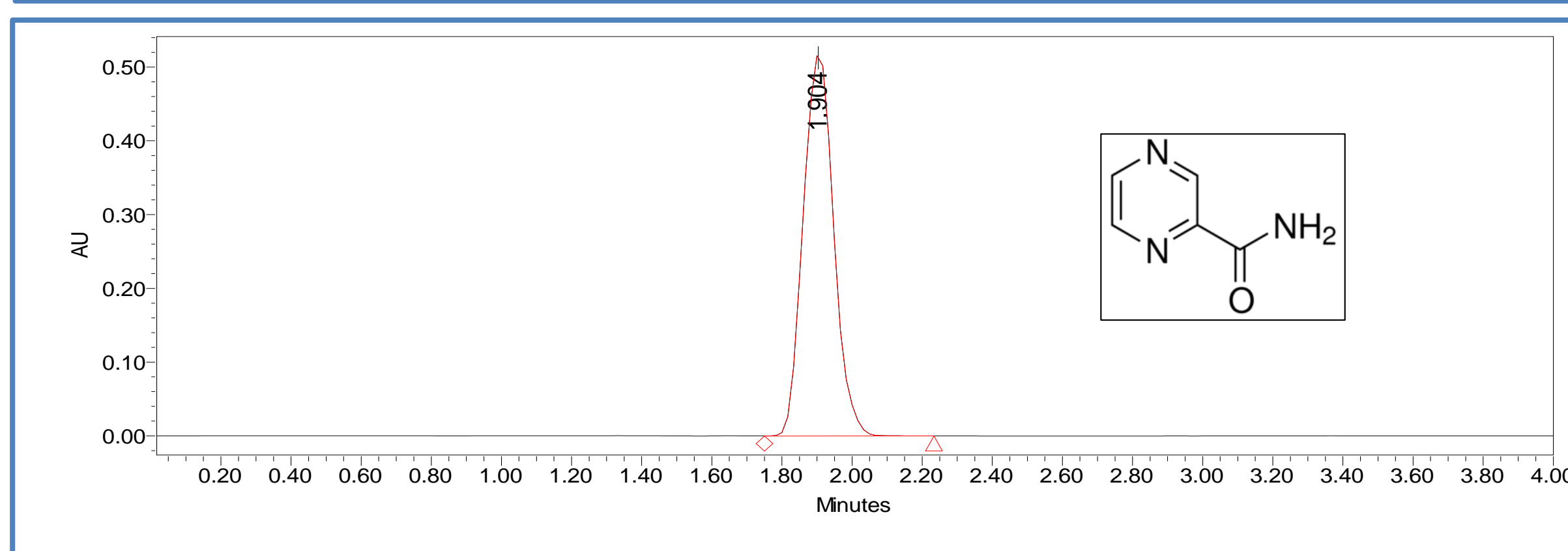
- ✓ Microbiological media plates remained free of any bacterial and fungal colony

Chemical stability



- ✓ No degradation product

Chromatogram of PZA (270 nm)



Analysis Time (Days)	95% confidence interval of the mean (100 mg/ml)
D0	96.61 < X < 100.82
D3	98.28 < X < 103.69
D5	95.20 < X < 100.69
D8	95.27 < X < 101.73
D15	95.46 < X < 102.59
D30	96.97 < X < 101.93
D60	99.75 < X < 104.92
D90	96.87 < X < 104.33

CONCLUSION

Finally, 100 mg/mL pyrazinamide oral suspension in Syrspend® SF PH4 is stable for at least 90 days at room temperature, so we determine a shelf life of 90 days for this preparation. Eventually this oral suspension could be used in children with tuberculosis infection throughout all the treatment duration usually recommended (3 months).