ATC code : N05- PSYCHOLEPTICS
Abstract Number : 3PC-006

STABILITY STUDY OF CLOBAZAM LIQUID ORAL FORMS FOR PEDIATRIC PATIENTS

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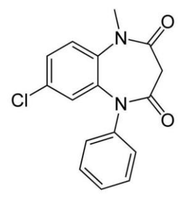


BACKGROUND AND IMPORTANCE

Clobazam is a benzodiazepine used as an **anti-epileptic drug** for pediatric patients.

- Several **supply difficulties** and even **stock-outs** of the oral suspension specialty for pediatric use.
- This treatment **can't be interrupted** during a supply disruption and treatment initiations can't be suspended for this indication.

As pediatric doses are weight-adjusted, the **development of a liquid formulation** was necessary to handle this supply issue.

AIM AND OBJECTIVES

Determine the **stability of Clobazam drinkable forms at 2 mg/mL** in two different commercial compounding excipients.

MATERIALS AND METHODS

Two formulations of Clobazam 2 mg/mL

Inorpha®

Syrspend® SF PH4 liquid

Three batches of each formulation:

- packaged in amber glass vials
- stored at **25°C ± 2°C** with relative humidity at **60% ± 5%**

Physical stability:

Organoleptic properties (visual appearance)

Chemical stability:

- **Measure of pH** (pHenomenal® VWR pHmeter)
- **Measure of osmolality** (Advanced Instruments Model 3250® Osmometer)
- **Quantification of Clobazam content and detection of degradation products**
  - *Validated stability-indicating method (according to ICH Q2R1)*
  - *Analytic method parameters*
    - HPLC with UV detection (λ=210 nm)
    - Column: Waters XSelect® HSS T3 (100 x 2.1 mm ; 2.5 µm)
    - Mobile phase: Water / Acetonitrile (55:45) (v/v)
    - Flow rate: 0.4 mL/min
    - Column temperature: 25°C
    - Injection volume: 2.5 µL

Study period (Days): D0 | D7 | D14 | D28 | D56 | D84

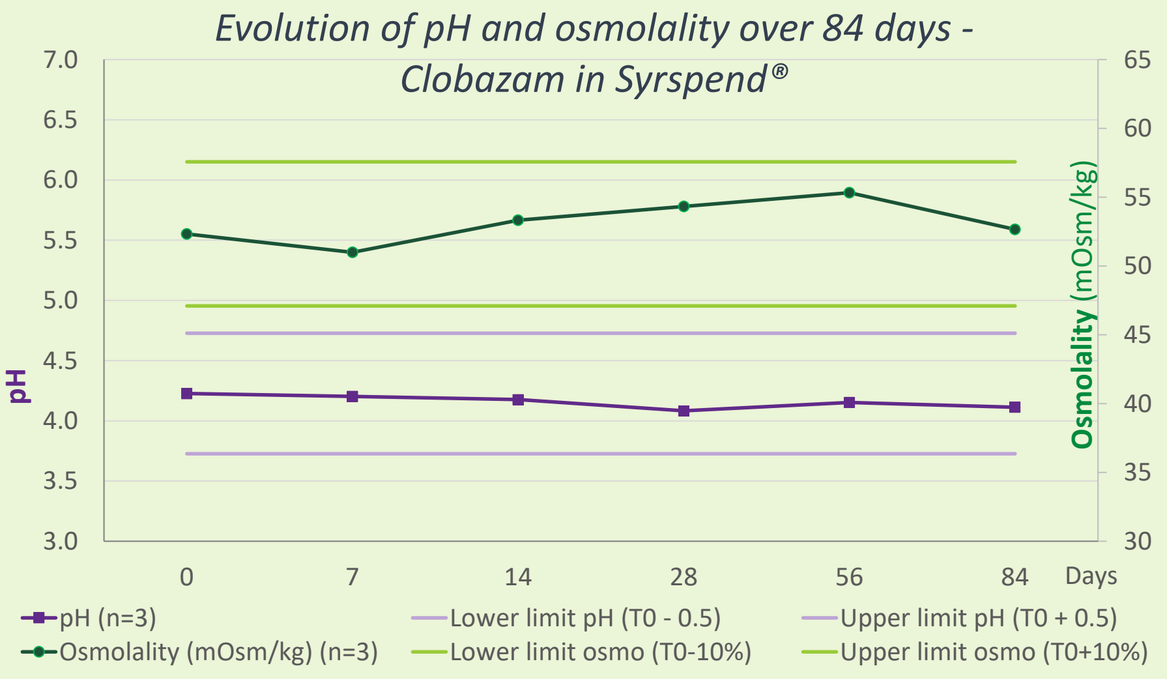
RESULTS

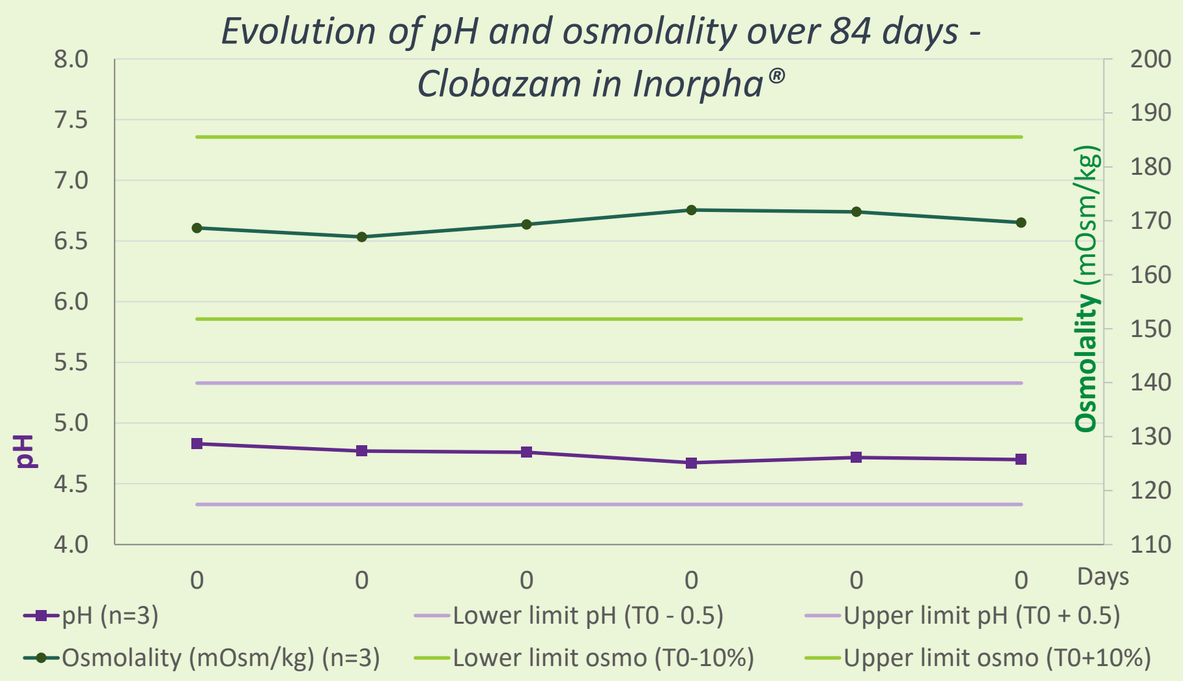
Physical stability:

✓ Aspect remained unchanged (visual, scent).

Chemical stability:

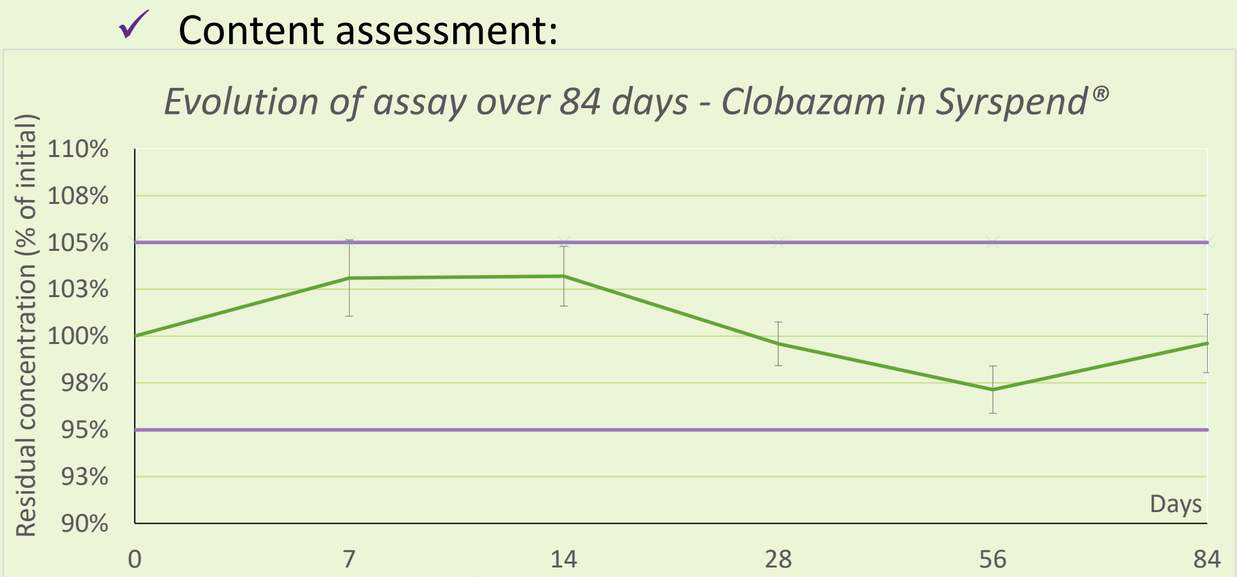
✓ Osmolality and pH assessment:

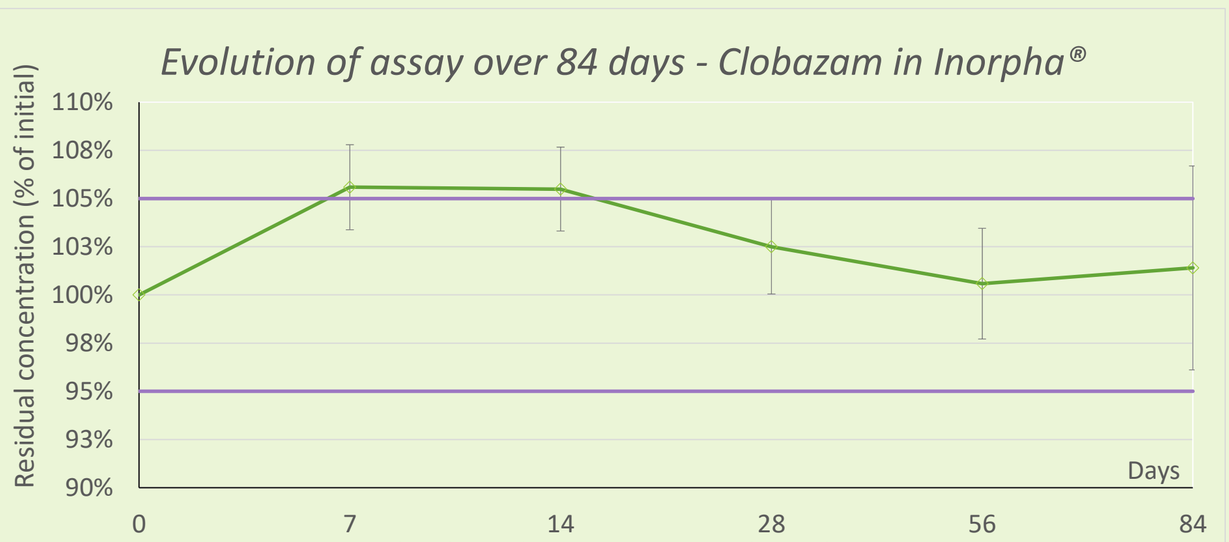




Osmolality and pH remained **stable** in both formulations.

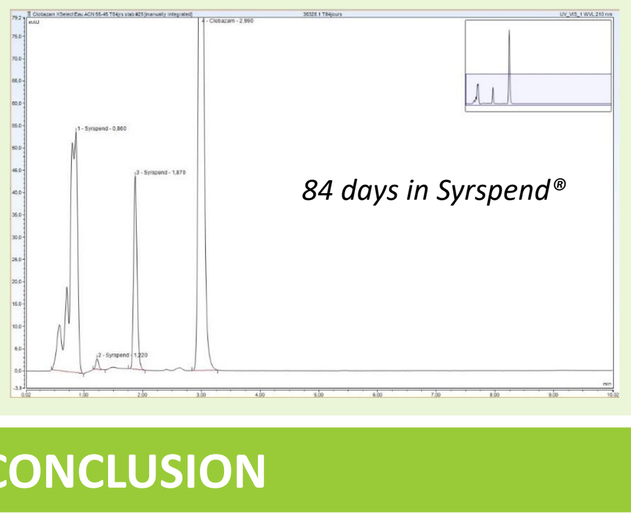
✓ Content assessment:

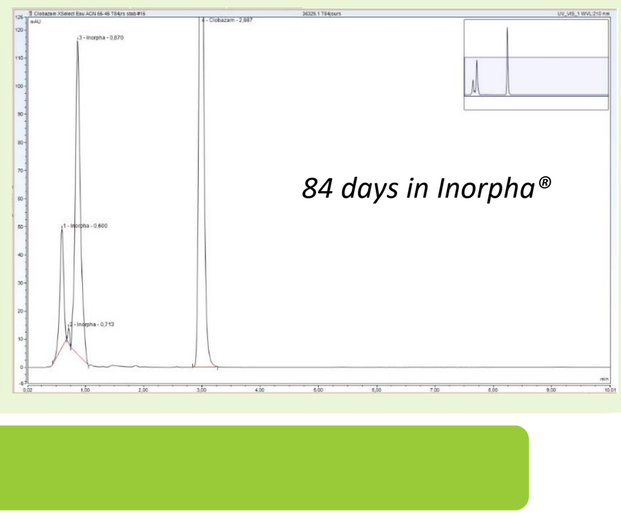




At Day 84, **the Clobazam concentration** of both formulations **remained above 95% of the initial concentration**.
A sedimentation with Inorpha® was observed, which explains interdays variability.

✓ No degradation product was observed.





CONCLUSION

A **Clobazam drinkable forms** at 2 mg/mL **can** therefore **be produced** in either Syrspend® SF PH4 or Inorpha® and **stored for 84 days at 25°C**, protected from light in case of supply shortage.
The formulation with Syrspend® seems to guarantee a better homogeneity due to viscosity.