Stability study of Letermovir in solution in 0.9% NaCl polypropylene bags

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Background

Letermovir (LTR) is an antiviral agent used for the prophylaxis of CMV infections in HSC transplants, for several days to weeks. The physico-chemical stability of the injectable form indicated by the manufacturer is 48h at 25°C in 0.9% NaCl or 5% Glucose, at a concentration of 0.9 and 1.8 mg/mL. In order to optimize the production of LTR bags, the physico-chemical stability of LTR was studied.

Materials & methods

Chromatographic conditions :
- C18 reverse phase column (15 cm x 2.1 mm ; 5 µm)
- Mobile phase : ammonium carbonate / ACN (60/40)
- Flow rate 0.300 mL/min ; thermostat 30°C ; injection 10µL
- DAD detector

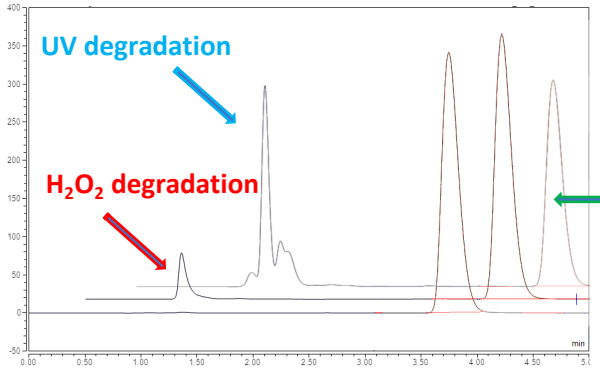
Dosage :
- at λ = 260 nm : calibration standards 25 - 50 - 75 µg/mL
- at λ = 260 nm : validation standards 38 - 49 - 58 µg/mL
- 190 to 400 nm scan : detection of LTR degradation products after exposure to UV, HCl, NaOH et H_2O_2

Storage conditions :
- 3 LTR concentrations, each in triplicates : 1 – 1.5 - 2 mg/mL
- LTR diluted in 0.9% NaCl polypropylene bags
- UV-protected bags stored at room temperature

Results

1) The analytical method is stability-indicating and complies with GERPAC recommendations :
=> specific, linear (R^2 > 0,99), repeatable (CV < 5%) and accurate (recovery ≈ 100%)

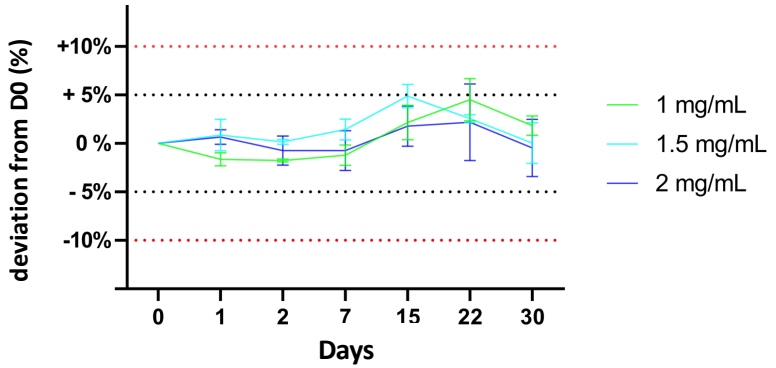
2) Detection of degradation products after UV and H_2O_2 exposure



Overlay chromatogram
λ = 260 nm

LTR
t_r ≈ 3.7 min

3) LTR stability over time :



Chromatogram :
- No degradation product

Physically :
- no visible particles (mirage test)
- transparency remains unchanged

Conclusion

The physico-chemical stability of LTR solutions of 1 to 2 mg/mL in 0.9% NaCl polypropylene bags, protected from UV light and at room temperature, is confirmed for up to 30 days after dilution of the injectable speciality.