Poster No.: 3PC-037

FORMULATION AND STABILITY OF LOSARTAN 0.8 MG/ML EYE DROPS FOR TREATMENT OF CORNEAL HAZE

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Background and Importance

Corneal haze is a term describing the loss of corneal transparency and associated with pathological wound healing after photorefractive keratectomy, eye injury, or eye infections. Recently the topical use of losartan potassium 0.8 mg/mL eye drops administered six times daily over a period of six months was reported to be effective in treating corneal haze.[1] As there is no authorised medicinal product available, losartan potassium 0.8 mg/mL eye drops must be provided as hospital pharmacy preparation.

Aim and Objectives

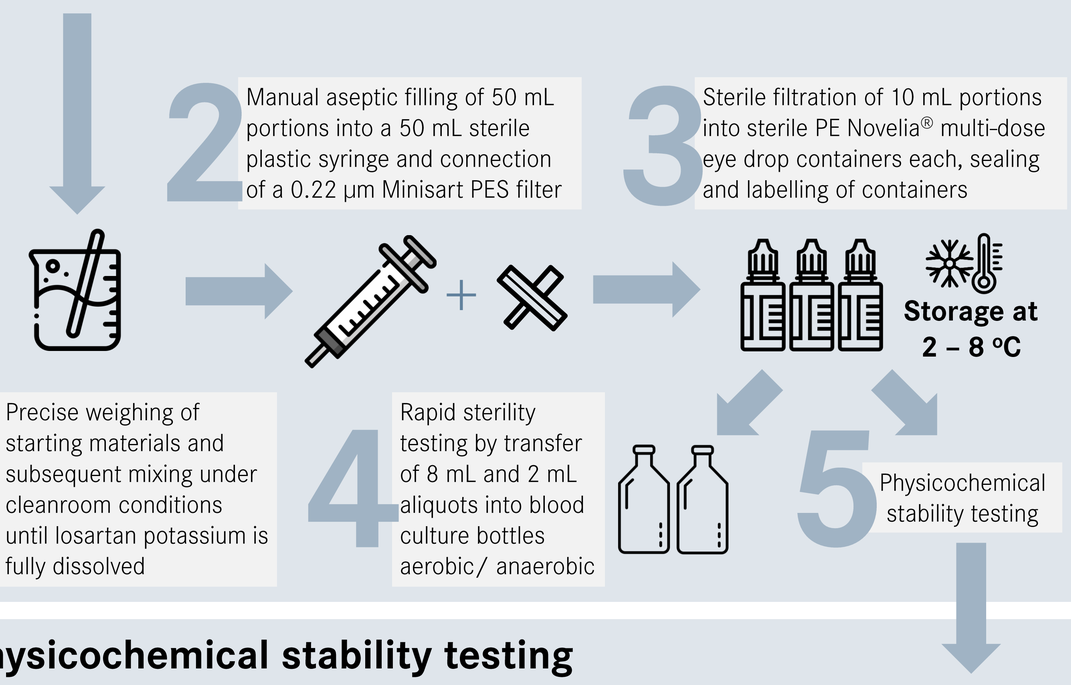
The aim of the project was the formulation, preparation, and stability testing of preservative-free losartan potassium 0.8 mg/mL eye drops in sterile polyethylene (PE) Novelia® multi-dose eye drop containers.

Materials and Methods

Preparation process of a qualification batch

Tab. 1: **Starting materials**

Losartan potassium API	0.130 g
0.9% sodium chloride sterile infusion solution	163 g



Physicochemical stability testing

- Sampling time points immediately (day 0), day 14, 28, 90

HPLC analysis of losartan potassium concentration

- Validated RP-HPLC analysis with photodiode array detector at 220 nm
- Column: µBondapak C18 10 µm, 300 x 3.9 mm
- Mobile phase: A: 80% KH_2PO_4 buffer (50 mM), 20% acetonitrile
  B: 70% KH_2PO_4 buffer (50 mM), 30% acetonitrile
- Gradient elution: 0-4 min 100% A; 4-6 min linear gradient to 100% B; 6-20 min 100% B
- Flow rate: 1.5 mL/min
- Temperature: 35 °C (column), 5 °C (samples)
- Injection volume: 20 µL in triplicate
- Runtime: 20 min
- Sample measuring concentration: 40 µg/mL losartan potassium
- Sampling: 3 containers diluted in triplicate and measured in triplicate each (n = 27)

pH and osmolality measurement (n = 3)

Results

Tab. 2: **Losartan potassium concentration in losartan potassium 0.8 mg/mL eye drops stored at 2–8 °C over 90 days**

Losartan potassium concentration [mg/mL] ± RSD [%] n = 27		Percentage rate of initial losartan potassium concentration (T0 = 100%) [%] ± RSD [%] n = 27		
Nominal	day 0	day 14	day 28	day 90
0.8	0.843 ± 1.06	100.16 ± 0.99	99.33 ± 0.94	94.31 ± 1.21

Tab. 3: **pH value and osmolality of prepared losartan potassium 0.8 mg/mL eye drops stored at 2-8 °C over 90 days**

	day 0	day 14	day 28	day 90
pH n = 3	6.3	6.3	6.2	6.2
Osmolality [mOsmol/kg] n = 3	288	291	288	287

- No significant changes of losartan concentration, pH and osmolality over a 3-month period of refrigerated storage
- Sterility tests showed no growth of bacteria and yeasts

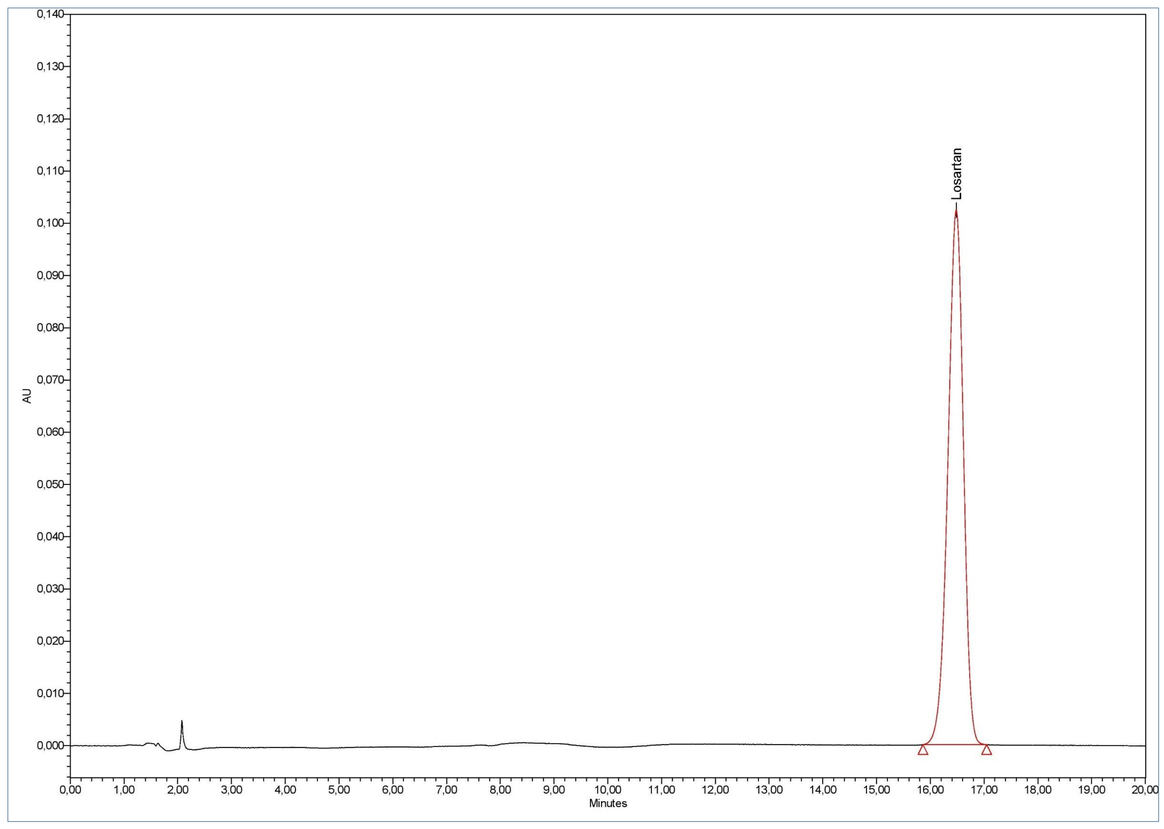


Fig. 1: **Example HPLC chromatogram of losartan potassium 0.8 mg/mL eye drop sample**

Conclusion and Relevance

The preparation of preservative-free losartan potassium 0.8 mg/mL eye drops was successfully implemented. The PE Novelia® multi-dose eye drop container allows multiple administration of preservative-free solutions and efficient pharmacy preparation. Shelf life was proven for at least a 3-month period when containers are stored refrigerated at 2-8 °C.

[1] Abdelghaffar M et al. Topical losartan ophthalmic drops – a review of corneal wound healing and topical losartan for managing corneal haze and potential future indications. Graefes Arch Clin Exp Ophthalmol 2025;263:925-934.