

Background



Clonidine is a drug used for opioid withdrawal syndrome in infants.
Issue : Nowadays, no pediatric form are commercialise

Aim



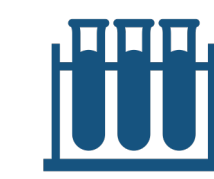
To provide a suitable and reproducible preparation to address the unavailability of a paediatric form at a 10 µg/mL concentration.

Materials and Methods



Formulation selection: literature research

The selection criteria included :
patient appropriate galenic form,
tolerance (pH, osmolarity),
absence of excipients with notable effects,
ease of preparation and dosage.



Development of analytical control:

performed by capillary electrophoresis



Method validation: SFSTP standards

accuracy profile at 3 concentrations:
6.3, 9.0, and 11.7 µg/mL over 3 days n = 3,
with acceptable limits defined at +/- 10%
and a beta proportion of 95%

Factors	Clonidine dosage	Excipients identification
Capillary length	8,5 cm (reverse capillary)	56 cm
Temperature	25° C	25° C
Voltage	-20 kV	-25 kV
Wavelength	200 nm	350 et 230 nm (reverse UV)
Injection pressure	-50 mBar for 5 sec	50 mBar for 6 sec
Buffer type	Phosphate 50 mM at pH 2,5	pH 12,1

Results



Formulation choice:

Selected solution

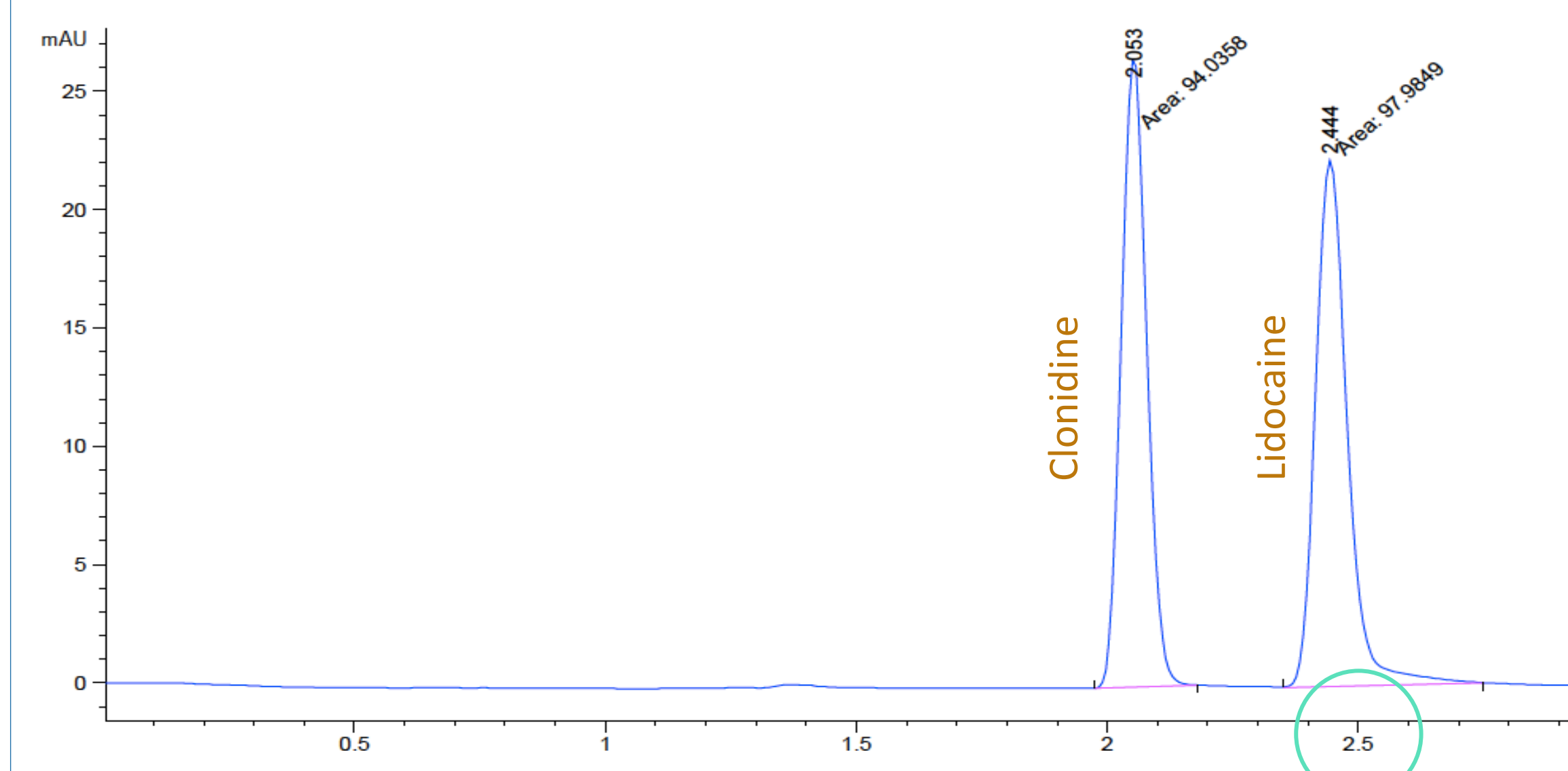
Criteria	Formula	Inorpha®	Saccharine solution	Simple syrup	Saccharose syrup	Selected Solution
Concentration		10 µg/mL	10 µg/mL	20 µg/mL	50 µg/mL	
Excipients with notable effects		2	1	1	yes	
Ease of preparation		+++	++	+	++	
Ease of dosage		+	+++	++	+++	
Physico-chemical stability		2 months at +4°C	3 months at +4°C 1 month at amb T°	3 months at +4°C	9 months at amb T°	
Bibliographical references		Potier A, Pharm Dev Technol. 2018 Dec;23(10):106-7-1076	Verlhac C, Pharm Technol Hosp Pharm. 2018;3(2):79-90	Merino-Bohórquez V, Pharm Dev Technol. 2019 Apr;24(4):465-478	De Goede A L, Inter J of Pharm. 2012 Aug;433(1-2):119-120	<ul style="list-style-type: none"> Potassium sorbate 300mg Potassium citrate 346mg Citric acid 200mg Saccharin sodium 26mg Water for injection sufficient quantity for 100mL



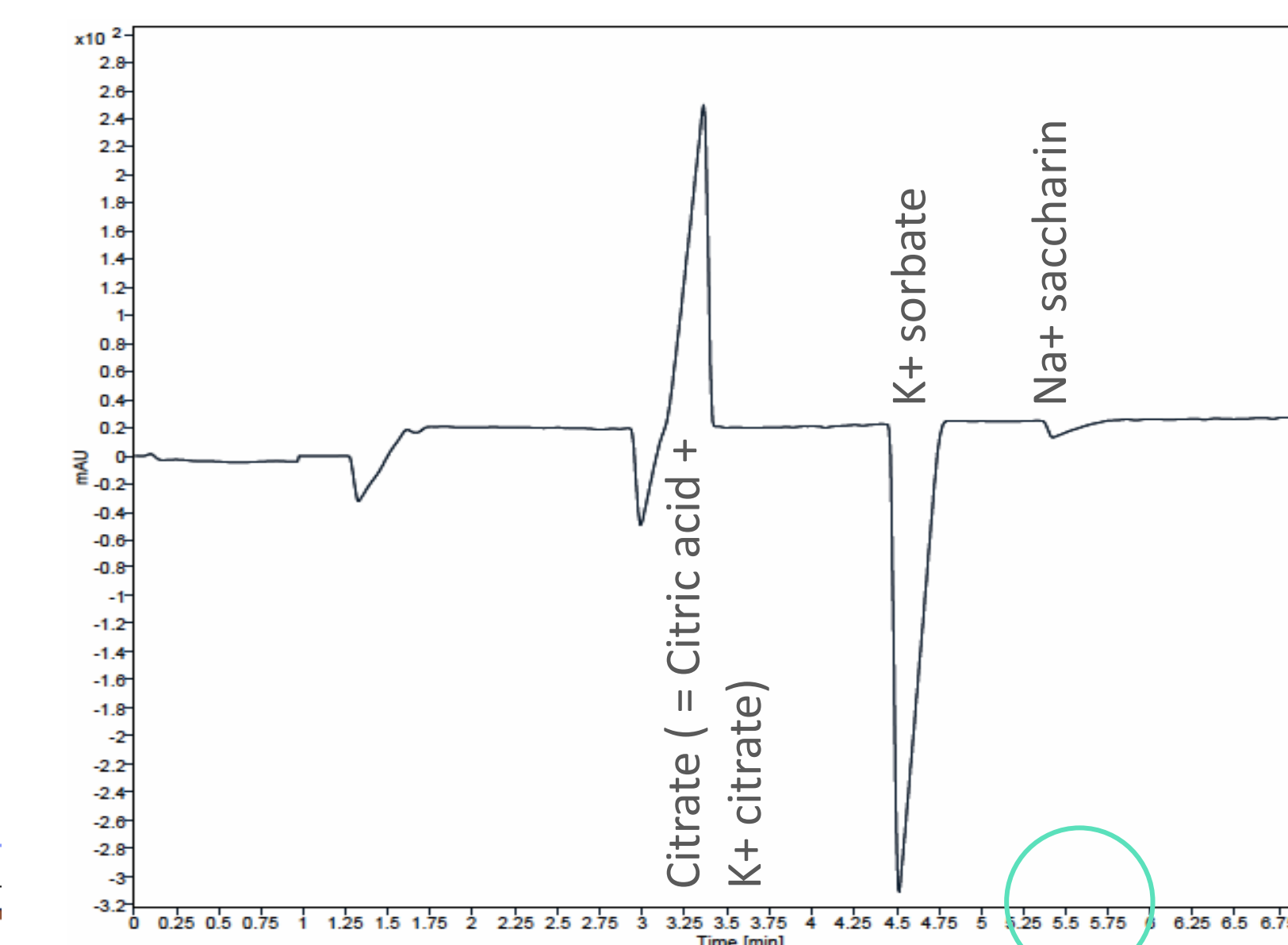
Analytical control

Clonidine analysis time < 3 min with the use of an internal standard (Lidocaine)

Coefficients of variation for repeatability and reproducibility < 5%

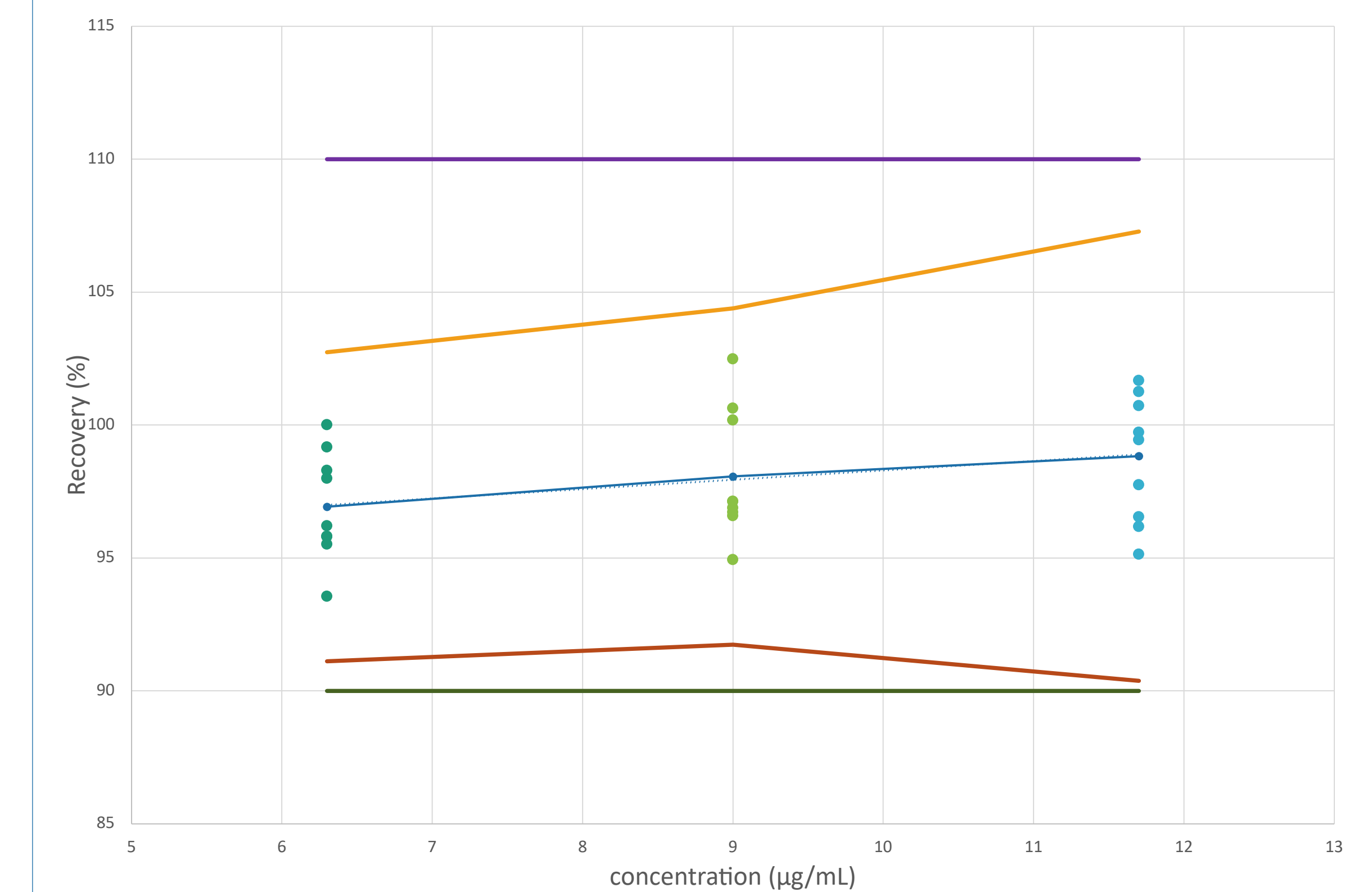


Excipients analysis time < 7 min



Accuracy profile

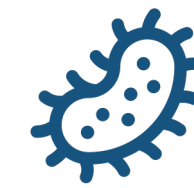
- recovery at 6.3 µg/mL
- recovery at 9.0 µg/mL
- recovery at 11.7 µg/mL
- average recovery
- tolerance interval lower limit
- tolerance interval higher limit
- low acceptability limit
- high acceptability limit



Discussion and Conclusion



An oral solution of pediatric clonidine can be made for a hospital prepatration and analyzed by capillary electrophoresis for batch release.



Physico-chemical stability is 3 months according to the bibliography, however microbiological stability should be demonstrated by a microbial enumeration test.