

INTRODUCTION

Phosphomannomutase 2 deficiency (PMM2-CDG) is the most common congenital glycosylation disorder, causing severe cerebellar developmental disorders with a highly variable phenotype depending on the patient. There is currently **no cure**, but several clinical studies show that epalrestat, an antidiabetic drug **not currently marketed in Europe**, could be effective in treating the cerebellar symptoms of this condition. A clinical study on the repositioning of this drug for this indication is currently being developed.



Develop and validate an HPLC-UV assay method in order to begin a feasibility study for the preparation of epalrestat capsules.

MATERIALS & METHODS

METHOD VALIDATION



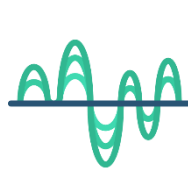
Mobile phase
Acetonitrile/Phosphate
buffer 25mM pH6,5 (32/68)



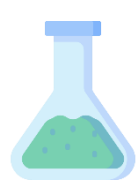
Stationary phase
Polaris® C18 column



HPLC ThermoFischer®
Polaris® C18 column

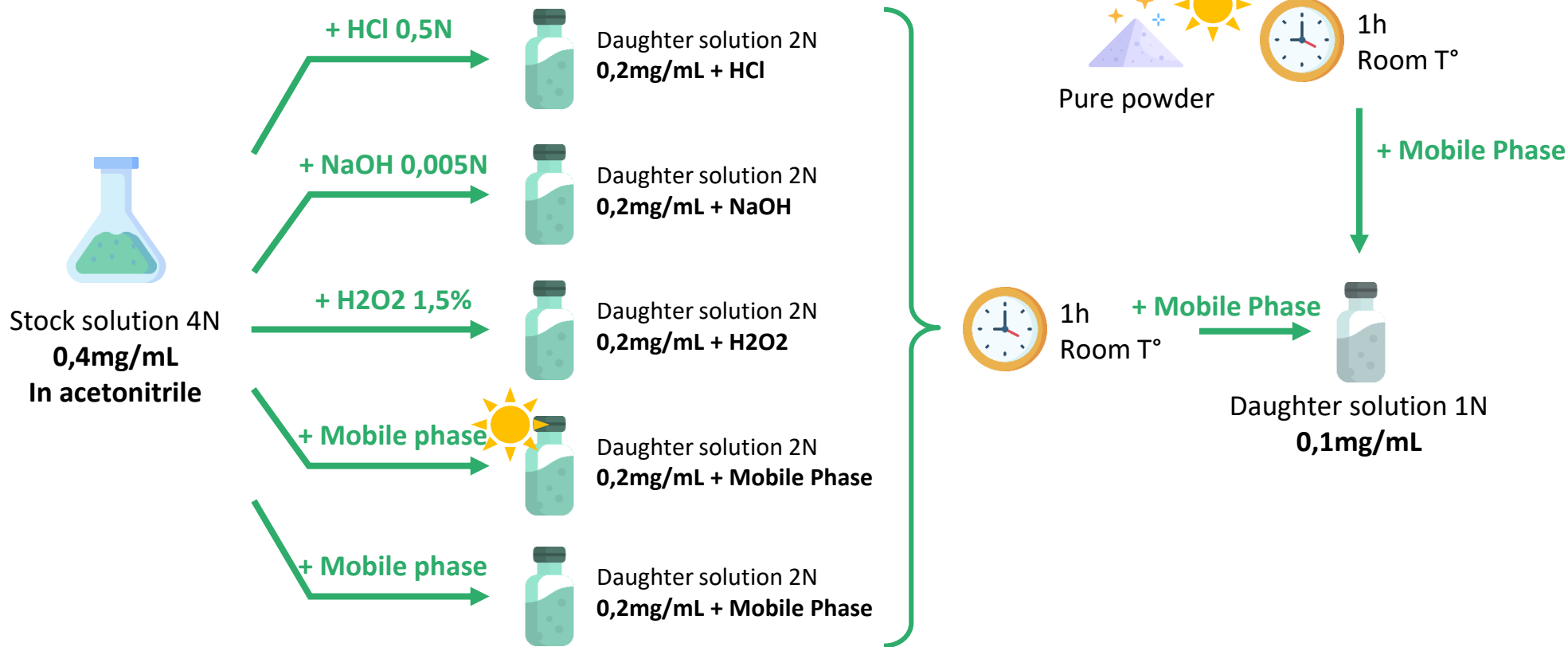


UV detector
395nm



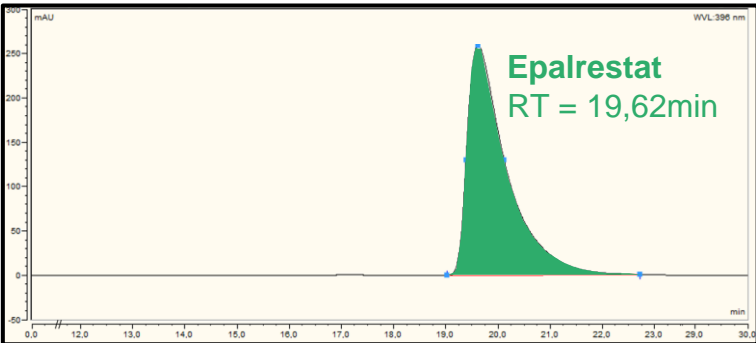
Range : [0,08 – 0,12] mg/mL
QC : 0,85 – 0,10 – 0,15 mg/mL

FORCED DEGRADATION

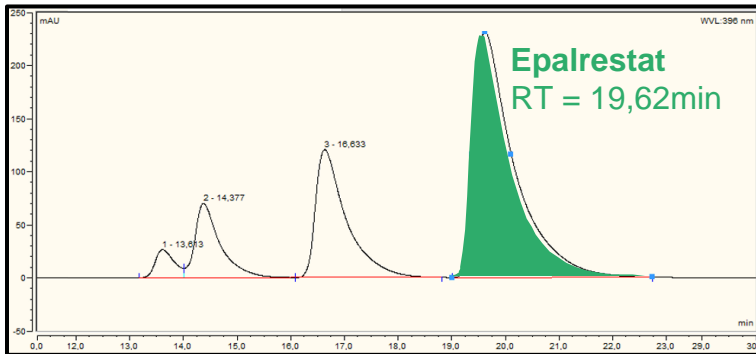


RESULTS

Method validation			
Linear equation	Y = 3827,7x - 4,741 AND slope : 137,24 AND y-intercept: 13,8		R² = 0,984
	QC1	QC2	QC3
Accuracy (Mean ± SD, n=9)	0,090 mg/mL ± 0,002	0,099 mg/mL ± 0,003	0,115 mg/mL ± 0,004
Intermediate precision (ER, n=9)	0,46%	-0,78%	-0,32%
Repeatability (CV, n=10)	0,26 %		
Quantification limit	0,036 mg/mL		
Detection limit	0,012 mg/mL		

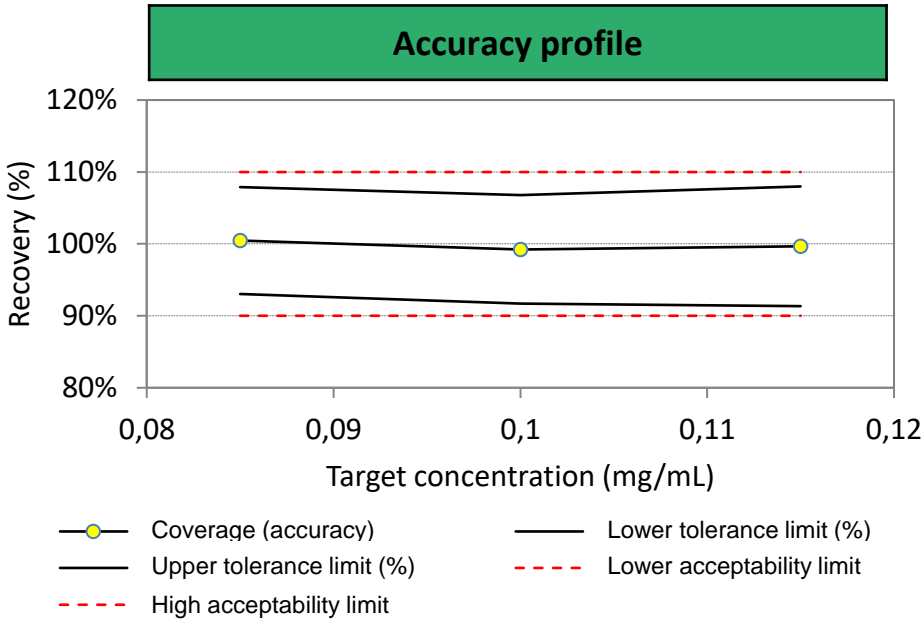


Chromatogram of epalrestat



Chromatogram of epalrestat degraded by light (1 hour)

Forced degradation					
	HCl 0,5N	NaOH 0,005N	H2O2 1,5%	Light solution	Light Powder
Degradation	77,1%	57,9%	91,0%	26,8%	-
RT of degradation product	13,5min 14,3min 16,6min	16,8min	6,4min 11,1min	13,6min 14,3min 16,6min	-



DISCUSSION/CONCLUSION

The method **has been validated** according to the criteria of international guideline ICH Q2 (R1) and allows for the establishment of an **epalrestat dosage**. Inter-day variability remains high. The handling protocol needs to be optimized. The stability study and galenic formulation can begin.