Development and validation of a method for the determination of Topiramate by HPLC-CAD

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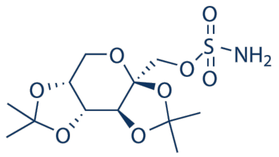
BACKGROUND AND OBJECTIVE

- Topiramate (TPR) is indicated for the management of epilepsy in children and adults.
- No speciality available for the paediatric population
  → TPR 6 mg/ml oral suspension formulation
- Molecule with no chromophore group
  → Use of conventional methods (e.g. HPLC-UV) not possible



Objective: To develop and validate a stability-indicating HPLC-DAC assay method for quality control of TPR oral suspensions, enabling efficient separation of TPR from its major impurities as described by *Eur.Ph.* , which are also its main degradation products

MATERIALS AND METHODS

1 **Development of dosing method**

- Literature review
- Choice of stationary and mobile phases
- Apparatus parameterization
- Comparison of chromatograms of TPR and impurities (*Eur.Ph.*)
- Excipients (Evaluation of matrix effect)

2 **Validation of dosing method**

- According to ICH Q2 and SFSTP recommendations

Chromatographic system : Vanquish (Thermofisher scientific®)

Protocol : over 3 days and by 3 separate operators

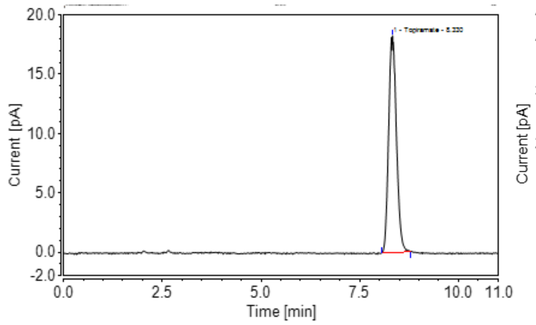
- ✓ Target concentration : 0,1 mg/ml
- ✓ 3 five-points ranges : **0,05 ; 0,08 ; 0,1 ; 0,12 ; 0,15 mg/ml**
- ✓ 3 QC levels : **0,08 ; 0,1 ; 0,12 mg/ml**

RESULTS

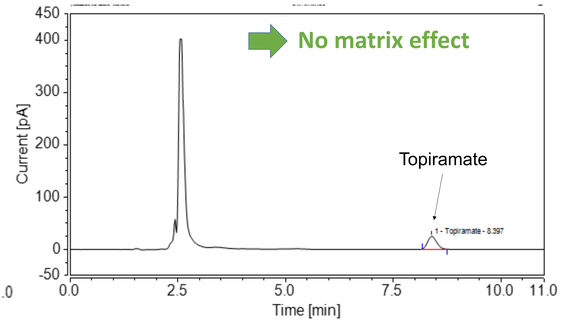
Chromatographic parameters

Phase mobile	Débit	Colonne	Température CAD	Pression	Volume d'injection
Eau/Méthanol (50/50 ; v/v)	1 ml/min	Agilent® Zorbax, Eclipse XDB-C18 (4,6x250mm, 5µm), 30°C	35°C	170 bar	20 µl

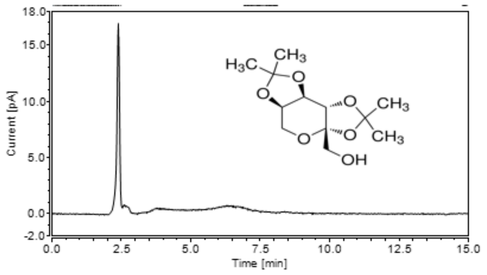
Topiramate CQ2: C = 0.1mg/ml



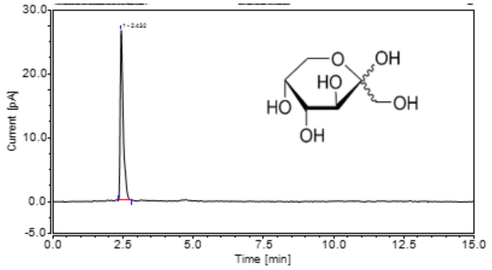
Topiramate C=0.1 mg/ml diluted in matrix



Impurity A



Impurity E



No interference of the TPR signal with its impurities

DISCUSSION / CONCLUSION

- Accurate, reliable and repeatable HPLC/CAD method for TPR determination
- No matrix effect observed
- Limitations: forced degradation difficult to follow in CAD

This work will continue with a stability study of TPR oral suspensions at 6 mg/mL formulated.

Method validation

Parameters	Results
Retention time	8,3 min
Linearity	$R^2 > 0,99$
	y = 34,58x + 0,71
Exactitude	Average coverage : R = 101,13 %
	IC95% : [100,15 % ; 102,12 %]
Repetability	CV = 0,73 %
Intermediate loyalty	CV = 4,0 %

Accuracy profile