Stability study of sildenafil capsules by High Performance Liquid Chromatography

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INTRODUCTION / OBJECTIVES

Sildenafil, phosphodiesterase V inhibitor, is used in pediatrics to treat pulmonary arterial hypertension. However no pediatric formulation was available until the recent launch announcement of a powder for oral suspension . The pharmacy of Lille Teaching Hospital is therefore preparing sildenafil capsules for pediatric dilutions.

According to « Bonnes Pratiques de Préparation », a French guideline published by the health authorities (ANSM), a preparation expiry date cannot exceed 28 days if its stability has not been investigated. The objective of this study is to determine the stability of sildenafil capsules at 1mg, 5mg and 10mg at room temperature, which would allow the pharmacy to prepare bigger batches with an extended expiry date. A HPLC assay has been developed and validated for this purpose.

METHODS

SILDENAFIL DOSING METHOD[1]

- Reverse phase HPLC
- Performed at room temperature using a Shimadzu LC-20AD pump with a Rheodyne injection valve of 10µL and a PerkinElmer UV series detector set at 240 nm
- Signal integrated with a Shimadzu CBM-20A integrator
- µbondapak Column C18 (10µ) 125A (3.9 x 300mm) and Prep column
- Mobile phase : acetonitrile / ammonium acetate 0.2M (50/50) with a flow set at 1mL/min

STABILITY STUDY

Capsules prepared with sildenafil citrate and corn starch at 1mg, 5mg and 10mg in sildenafil base kept at ambient temperature in transparent blister packs sealed with aluminium foil

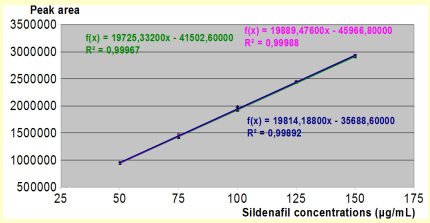
Checks carried out

- Uniformity of mass at D0
- Capsules visual aspect, sildenafil concentrations and chromatographic profiles on 2 samples at D0, D7, D14, D21, D35, D42, D56 and D70

RESULTS

METHOD VALIDATION

Linearity



Correlation coefficient > 0,99
Linearity for sildenafil concentrations from 50 to 150 µg/mL
Relative standard deviation = 1,53% (< 2%)

Specificity

Corn starch addition does not affect sildenafil peak surface and retention time.

Repeatability

Sildenafil concentration (µg/mL)	60			100			140		
Day of analysis	D1	D2	D3	D1	D2	D3	D1	D2	D3
Standard deviation (%)	1.5998	1.6782	1.3748	1.7473	0.7721	0.5688	0.4581	1.0786	0.5637

Standard Deviation < 2 %

Intermediate precision

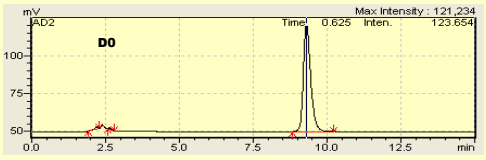
Sildenafil concentration (µg/mL)	60	100	140
Standard deviation (%) D1+D2+D3	1.8336	1.2415	1.4036

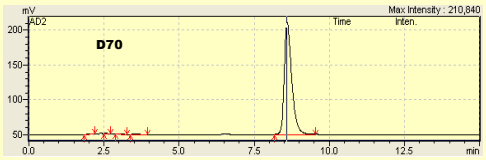
Standard Deviation < 2 %

THE METHOD IS VALIDATED

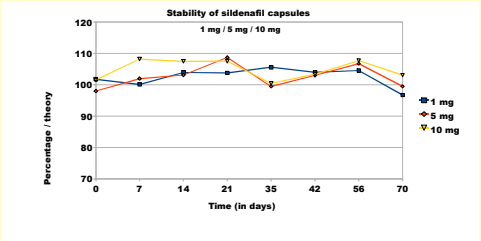
STABILITY STUDY

- Uniformity of mass verified at D0
- No change in capsules visual aspect from D0 to D70
- No significant change in chromatographic profile from D0 to D70





- Percentages of the remaining concentrations of sildenafil in the capsules are over 90 % after 70 days.



Sildenafil concentration is expressed as the percentage of the remaining drug concentration at different days. The measured concentration is the average of 2 replicates. The stability is assumed if the loss is less than 10% of the theoretical concentration.

DISCUSSION / CONCLUSION

The method has been validated and used in a stability study which demonstrated the stability of sildenafil capsules up to ten weeks under the studied storage conditions. These results allowed us to prepare in advance large number of sildenafil capsules with a shelf-life of eight weeks, which ensures an immediate availability of this medication for the patient and improves the pharmacy workload .

1 Developed from Daragmeh N. et al. Determination of sildenafil citrate and related substances in the commercial products and tablet dosage form using HPLC. J Pharm Biomed Anal. 2001;25:483-492