Stability study of sildenafil capsules by High Performance Liquid Chromatography

M. Lebecque, H. Beaussart, C. Berneron, P. Odou

Regional University Hospital, department of Pharmacy, Lille, France
Faculty of pharmaceutical and biological Sciences, Lille, France

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 METHOD¹
- Reverse phase HPLC
- Performed at room temperature using a Shimadzu LC-20AD pump with a Rheodyne injection valve of 10 µL and a PerkinElmer UV series detector set at 240 nm
- Signal integrated with a Shimadzu CBM-20A integrator
- Mobile phase: acetonitrile / ammonium acetate 0.2 M (50/50) with a flow set at 1mL/min
- µbondapak Column C18 (10 µM) 125A (3.9 x 300mm) and Prep column
- Signal integrated with a Shimadzu CBM-20A integrator

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

Peak area

<table>
<thead>
<tr>
<th>Sildenafil concentration (µg/mL)</th>
<th>50</th>
<th>100</th>
<th>150</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear correlation coefficient</td>
<td>0.99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linear fit of sildenafil concentractions from 50 to 150 µg/mL</td>
<td>Relative standard deviation = 1.53% (&lt; 2%)</td>
<td></td>
<td></td>
</tr>
</tbody>
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Specificity

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

Repeatability

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<td>Intermediate precision</td>
<td>1.039</td>
<td>1.202</td>
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<td>Standard Deviation (%)</td>
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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.

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.