

Stability studies with levosimendan-syringes

Introduction

Levosimendan (Simdax®) is a calcium sensitizer which is effective in treatment of heart failure. The available vials contain an adult dose, but levosimendan is also used as off label therapy in children.

Aseptic preparation of low doses of levosimendan safe costs. We have already demonstrated the chemical stability of levosimendan [1]. Because preparations in syringes, specially of more volatile and lipophilic solutions are problematic, we now also focused the leachables out of polypropylene syringes. A syringe is not a totally closed system for volatile solvents and the risk of leachables is higher with lipophilic solvents.

Results

Stability data

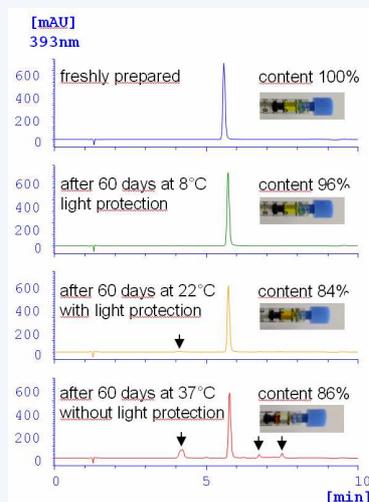


Fig. 1: Chromatograms with the „stability method“
↓ = main degradation products

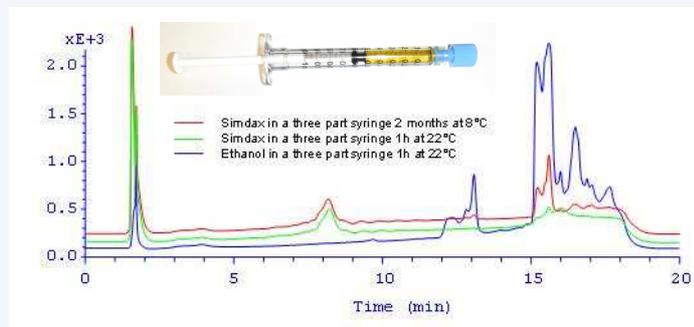
Materials and Methods

Stability Method: Nucleodur 100-5 C18ec column, gradient with Phosphatebuffer pH5/Methanol (30-80% Methanol). All UV detectable degradation products of levosimendan after different stress tests could be separated. Validation was performed according to the guidelines for practical stability studies [2].

Leachable Method: Nucleodur 100-5 C18ec column, gradient with Phosphatebuffer pH5/Methanol (30-100% Methanol).

More details can be requested from the authors.

Detection of a yet unknown leachable



Possible Solution

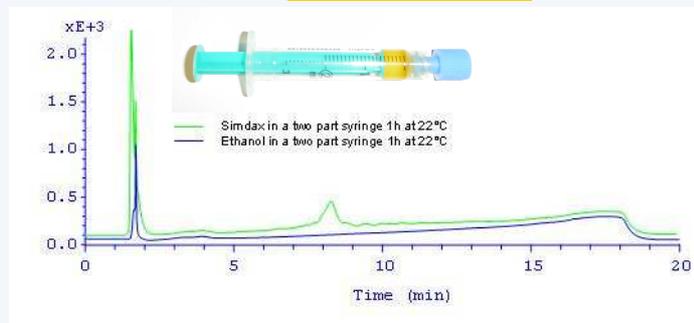


Fig. 2: Chromatograms with the „leachable method“ at 210nm

Summary of Results

We could confirm our former results about the chemical stability with a second batch of Simdax®. After 2 months no degradation products could be detected in the samples prepared in 1ml three part syringes. With a gradient to 100% methanol unknown leachables could be detected. In 3ml two part syringes no leachables were found.

Conclusions

If a microbiological validation of the aseptic preparations is done, an in-advance-preparation of levosimendan child-doses in the pharmacy is possible. The preparations are stable for 2 months if they are stored at 8°C. This leads to a relevant economizing of child's therapy with levosimendan. Because of detectable leachables (already after 1h!) in three part syringes, special care needs to be taken in the choice of the containers. The relevance of these leachables/extractables needs further investigation.

Literatur:

- [1] R. Trittler, J. Hecklinger, MJ Hug. Aliquotierte Levosimendanlösungen – stabil? Poster auf dem ADKA Kongress in Dresden 2013
[2] C. Bardin, A. Astier, A. Vulto, G. Sewell, J. Vigneron, R. Trittler, M. Daouphars, M. Paul, M. Trojniak, F. Pinguet. Guidelines for the practical stability studies of anticancer drugs: A European consensus conference. Annales Pharmaceutiques Francaise 2011; 69: 221-231