



Stability of 1 IU/mL diluted insulin solution: don't forget the preservatives!

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Introduction

A stability study has to follow the evolution of all galenic formulation components (drugs and excipients). Insulin (I) is precisely formulated with two preservatives: phenol (P) and metacresol (M). Even at very low concentration, these additives guarantee the best solution stability thanks to the hexameric structure of the protein (Teska et al. 2014). The aim of the study was to evaluate stability of 1 UI/mL insulin solution stored in syringes or AT-Closed Vials[®].

Methods

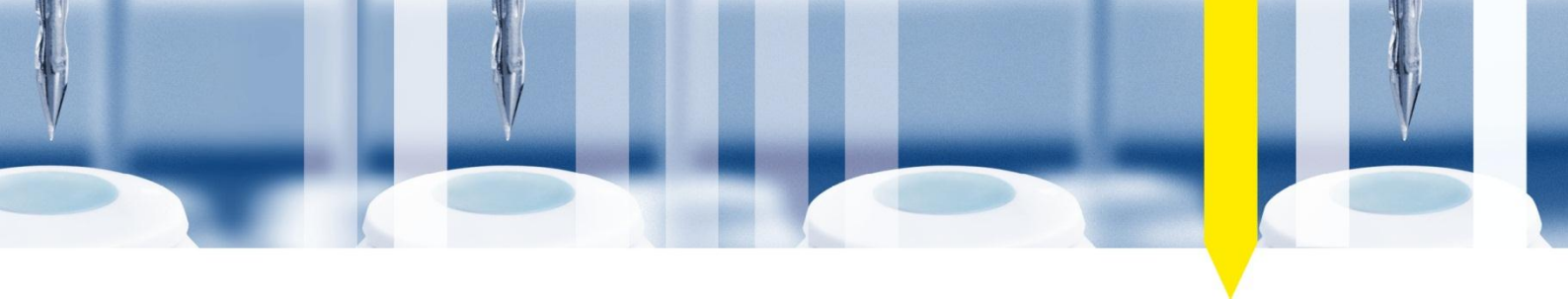
50mL of insulin aspart 1IU/mL (Novorapid[®], NovoNordisk), diluted in saline, were packaged in polypropylene syringes (Plastipak[®], Becton-Dickinson) or cyclic olefin copolymer AT-Closed Vials[®] (Aseptic Technologies) closed by two different formulations of stoppers (green and grey), stored at controlled room temperature (25°C/60%RH). The evolution of concentrations of I, P and M were determined by an HPLC-UV stability indicating method (n=6) and expressed as ratio of initial concentration (%). Solutions were considered as stable only if the three components stayed over 90%. Results were expressed as mean±standard deviation.

Results

Solution was stable during 30 days in syringes (I: 97.78±1.09%; P: 96.12±0.19%; M: 91.00±0.38%), 60 days in vials with green stoppers (I: 94.68±0.42%; P: 96.80±0.21%; M: 91.84±0.66%); despite insulin concentration was still over 90% after 75 days. In vials with grey stoppers, it was still stable after 90 days of study (I: 94.06±0.53%; P: 97.83±0.57%; M: 94.66±1.22%).

Discussion/Conclusion

This study highlights the interest in following all the components of a drug formulation. In a CIVAS context, the use of AT-Closed Vials[®] allowed a better conservation of metacresol and should be promoted to store 1 IU/mL insulin solution in the easiest storage conditions (room temperature). Stopper selection impacted on stability and has to be in accordance with physico-chemical



characteristics of excipients besides active drugs. Complementary analyses have to confirm impact of preservatives loss on insulin activity.

Source: <https://www.gerpac.eu/stability-of-1-iu-ml-diluted-insulin-solution-don-t-forget-the-preservatives>