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The stability of nanoliposomal cytostatic drugs – ONIVYDE pegylated liposomal (Irinotecan)

Introduction

Liposomal anticancer agents offer enhanced pharmacokinetic properties compared to their parent compounds, such as reducing the occurrence of unwanted off-target effects or extending plasma half-life [1]. As a result, the number of approved liposomal drugs continues to rise [2]. ONIVYDE pegylated must be diluted before administration, and compounding pharmacies are responsible for preparing the appropriate custom formulation and dosage. Once opened, proper in-use storage conditions and timeframes must be monitored by the user. The manufacturer guarantees the stability of diluted dispersions for up to 24 hours at 2-8 °C. Aseptic techniques should be strictly followed during infusion preparation. For undiluted ONIVYDE pegylated liposomal, single-use only is recommended [3].

Material and Method

The storage life of diluted and non-diluted ONIVYDE pegylated liposomal has been investigated after opening for an overall time interval of 28 days (n = 3). The stability of the cargo irinotecan has been studied before [4]. Thus, this study concentrates on the shelf life of the nanoliposomal carrier by monitoring the release of irinotecan. Therefore, ONIVYDE pegylated liposomal (4.3 mg mL^{-1} concentrate for dispersion for infusion) dilutions in were carried out inside infusion bags (0.2 and 0.3 mg mL^{-1} in 0.9% NaCl). To determine the stability of the stock solution and the dilutions were filtered using centrifugal filters and the concentration of irinotecan in the filtrate was measured using liquid chromatography with UV-detection and by visual inspection of the ONIVYDE pegylated liposomal containers. The analytical method was complete validated (linearity, within day and between day reproducibility, stability indicating capability and low variability).

Results and discussion

For three pharmaceutical phials, data were collected after 0, 1, 3, 7, 14, 21 and 28 days at 2-8°C. At this time period the release of irinotecan increases slightly from 4.1 to 7.9 µg mL^{-1}. In relation to the filtered cargo concentration a relative release of 0.1 to 0.2 % were measured. Similar results were achieved for the infusion bag. The release of irinotecan increased from 1.6 and 1.5 µg mL^{-1} to 3.4 and 3.7 µg mL^{-1} for the 200 and 300 µg/mL infusion bags, respectively. These results show a degradation of 1.7 and 1.3 % of the 200 and 300 µg mL^{-1} infusion bags, respectively. Therefore, a stability of diluted and non-diluted ONIVYDE pegylated liposomal for 28 days (>98%) is demonstrated.

Conclusion

We developed and validated a method focusing on the release of the cargo from its container to estimate the stability of drugs on the basis of pegylated nanoliposomes. We demonstrate the applicability on ONIVYDE pegylated liposomal as an example. Opened, diluted and non-diluted ONIVYDE pegylated liposomal shows a good stability for 28 days. Based on the stability data shown here, single use is not mandatory.

References:

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