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

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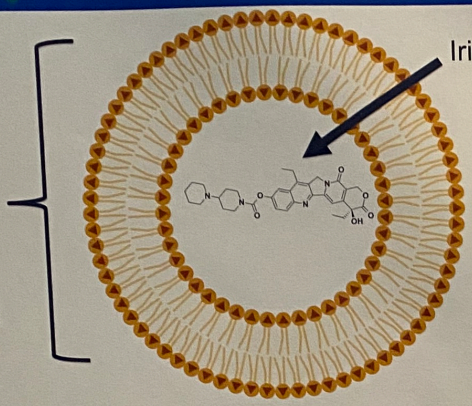
Introduction



Liposomal anticancer agents offer enhanced pharmacokinetic properties, 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].

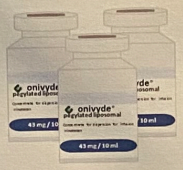
This study aims to investigate the stability of pegylated liposomal Irinotecan. Since the stability of Irinotecan is known to be longer, this study focuses on the release of free Irinotecan from the pegylated liposomal layer.

[1] Gerard, M.; Innocenti, F.; Minami, H. (2022) Cancer Science, 113 (7): 2224. DOI:10.1111/cas.15377
[2] Liu, P.; Chen, G.; Zhang, J. (2022) Molecules, 27, 1372. DOI: 10.3390/molecules27041372
[3] Onivyde pegylated liposomal: EPAR – Product information, last updated: 13/12/2022.

Results

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 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 % was measured (Figure 1).



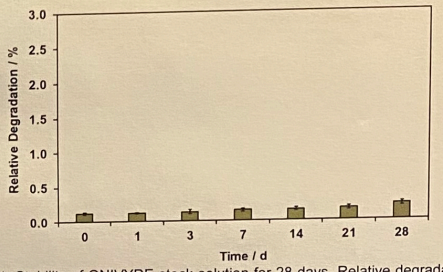
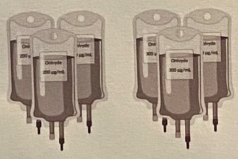


Figure 1: Stability of ONIVYDE stock solution for 28 days. Relative degradation was determined by release of free Irinotecan. All experiments were carried out in triplicates and the error bars represent the standard deviation of the results.

Infusion bags

- 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 from 1.6 and 1.5 µg mL^{-1} to 3.4 and 3.7 µg mL^{-1} in the 200 and 300 µg mL^{-1} infusion bag, respectively.
- In relation to the filtered cargo concentration a relative release of 1.7 and 1.3 % was measured in the 200 and 300 µg mL^{-1} infusion bag, respectively (Figure 2).



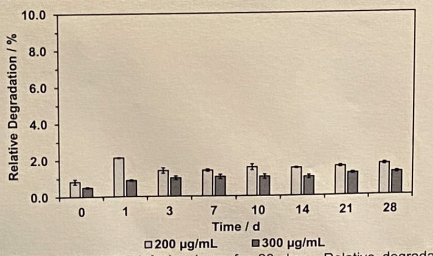
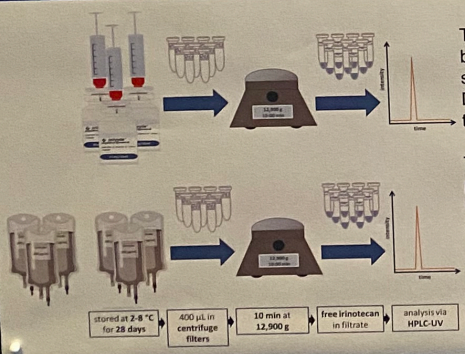


Figure 2: Stability of ONIVYDE infusion bags for 28 days. Relative degradation was determined by release of free Irinotecan. All experiments were carried out in triplicates and the error bars represent the standard deviation of the results.

This study demonstrated that the stability of pegylated liposomal Irinotecan (> 95%) is much longer than the manufacturer's guaranteed lifespan. Prolonged storage time reduces costs and waste.

Material and Method



The storage life of diluted and non-diluted ONIVYDE pegylated liposomal has been investigated after opening for 28 days (n = 3). This study focusses on the shelf life of the nanoliposomal carrier by monitoring the release of irinotecan. Dilutions of ONIVYDE pegylated liposomal, at concentrations commonly used in therapy, were prepared in infusion bags (0.2 and 0.3 mg mL^{-1} in 0.9% NaCl).

The samples were filtered using centrifugal filters to determine the stability of the pharmaceutical phials and the infusion bags. 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 fully validated (linearity, within-day and between-day reproducibility, stability-indicating capability, and low variability). The recovery of Irinotecan in lower concentrations ranged between 60 – 85 %.

Further questions?

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