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Application Note

Apparatus for Dissolution Testing of Lipid Nanoparticles

Introduction

Lipid Nano Particles, (LNPs), are being used and investigated for a wide variety of medical treatments. Vaccines, gene therapy, and anti-cancer drugs are among the candidates for this delivery method. They can also be used to deliver large molecule payloads such as mRNA. LNPs as carriers avoid issues of toxicity, solubility, allergic and immunogenic reactions. LNPs can also stabilize chemically labile formulations.

To date there has not been an effective way to assess the dissolution of drug from LNPs. Traditional dissolution apparatus assumes the dose is free to dissolve in the test medium, but with LNPs the active ingredient is sequestered in a lipid bubble. On analysis the lipid and active ingredient are analyzed together.

Is the drug free of the LNPs or still sequestered?

Logan Instrument Corporation has developed a method to separate the lipid from the active using a novel apparatus that can be utilized within a USP Apparatus 3 reciprocating rack system.

Description of Apparatus

The device consists of a stainless steel frame that supports a dialysis membrane. The LNP sample for investigation is contained within the membrane. The frame and membrane assembly with the LNPs is placed into the USP Apparatus vessel and the analysis run using a suitable protocol based on the formulation.

Experiment Purpose

To measure the cumulative release rate of paclitaxel liposomes using a novel Nano-Frame to support a dialysis bag. The Nano-Frame assembly is mounted within the System ADR III-7 reciprocating rack system of Logan Instruments Company.

Logan SYSTEM ADR III-7

Method

Reciprocal rack method: The nanomedicine dissolution system consists of a nanocage, paddle bar, dissolution vessels, multiple rows of racks, and a system controller. This method allows the use of multiple rows of dissolution methods. The reciprocating motion ensures homogeneous mixing of the sample solution in the nanocage and avoids sample adhesion to the dialysis membrane.

Nano-Frames inside dissolution vessels in ADR III-7 racks

Dialysis bag molecular weight: 100 kDa (flattening width: 16 mm, water injection diameter: 10 mm). Release medium: 40 mL of PBS solution containing 2% Tween 80 (wt%) Volume of preparation in dialysis bag: 1 mL, dialysis bags containing 0.4 mg (n=3) and 0.8 mg (n=3), respectively. Liposomes of PTX.

- First row sampling time point: 1 h, 2 h
- Second row sampling time point: 4 h, 8 h
- Third row sampling time point: 2 h,16 h
- Fourth row sampling time point: 20 h, 24 h
- Fifth row sampling time point: 36 h, 48 h
- Sixth row sampling time point: 72 h, 96 h
- Sampling volume: 1 mL
- Flush pipe volume: 9 mL
- Volume of prime: no prime
- Number of lifts per minute: 40 dpm
- Travelled distance: 2 cm
- Temperature: 37.2℃

The particle size of PTX liposomes within the 96 h Nano-Frame ranged from 115 nm to 164 nm.

Experiment Results

The cumulative percentages of release for the fourth day reciprocating rack method are shown in Figure 1.

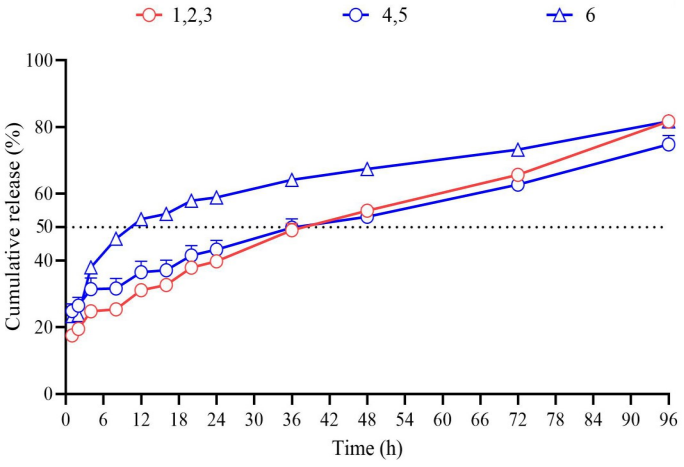

Figure 1 Cumulative release curve of paclitaxel lipids in 2% Tween 80 PBS solution using reciprocal rack method.

The release of Nano-Frames 1, 2, and 3 loaded with 0.4 mg PTX was slightly faster than that of Nano-Frames 4, 5, and 6 loaded with 0.8 mg PTX after 36h~96h, probably due to the greater difference in PTX concentration inside and outside the dialysis bags of numbers 1, 2, and 3.

The cumulative release at the release endpoint is about 82% for numbers 1, 2, and 3 and about 75% for numbers 4 and 5,

The reciprocating rack still showed a tendency to continue releasing at 96 h.

The release of number 6 was significantly faster than that of numbers 4 and 5 in the same group, probably because more liposomes leaked at the beginning of the experiment. The results showed that although number 6 leaked more at the beginning of the experiment, the release rate of PTX at 48 h~96 h was similar to that of 0.4 mg PTX loaded in the dialysis bag, and the release endpoint was 82%, indicating that the release conditions met the requirements of 0.4 mg PTX and 0.8 mg PTX loaded in the dialysis bag. Due to the effect of liposome leakage, before 36 h we used 36 h~96 h data for analysis.

Conclusion

The results show that the Logan Nano-Frame apparatus is a suitable method to measure the dissolution rate of active ingredients from nano particles. The method can be modified to suit different nanoparticle structures and experimental objectives by varying the specification of the dialysis membrane, media and mode of action of the apparatus. Investigations are underway to evaluate the technique with other USP Apparatus including USP 4 flow through systems.

For more information please contact Logan Instruments Corp. at info@loganinstruments.com or through our website www.LoganInstruments.com

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