How to assess drug release from micro- and nanosized carriers?

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INTRODUCTION

Today, investigating the *in vitro drug* release from dispersed micro- and nanoformulations is still challenging modern dissolution technologies. More often, it involves the separation of the dispersed carrier from the free drug by subjecting the formulation to mechanical forces[1] or by applying dialysis-based techniques [2].

While many sampling procedures entail the risk of disrupting the carrier structure resulting in a more rapid drug release, most dialysis procedures are not sensitive enough to discriminate between different formulations or batches [2]. In this context, the barrier properties of the dialysis membrane are rate limiting to the drug release. For this reason, the drug release test is the more sensitive, the higher the permeation rate of the drug through the dialysis membrane [3].

RELEASE TESTING OF MICRO- AND NANOFORMULATIONS

In the area of micro- and nanoformulations, fluctuations in the release profile are more likely due to the high surface area of these carriers. The dispersion releaser (DR) technology [4, 5] has been developed to conduct dialysis-based release experiments with dispersed carriers taking advantage of the compendial equipment described by the United States Pharmacopeia (USP), the European Pharmacopeia (EP) and the Japanese Pharmacopeia (JP). A high sensitivity of the measurement is achieved in quality control but also in presence of physiological fluids [6]. The dialysis cell of the DR is mounted into a dissolution vessel or mini vessel of the dissolution USP apparatus 2 (see figure 2, left).

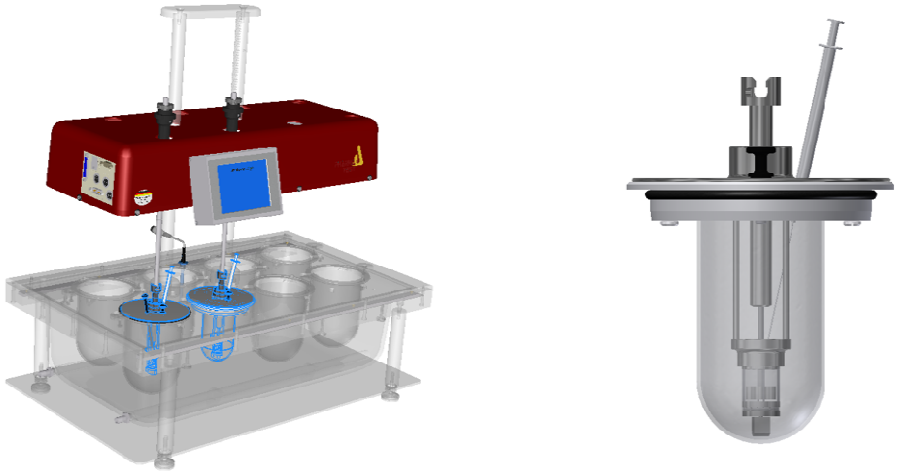

Figure 1: Schematic of the commercial dispersion releaser technology build into USP apparatus 2 with standard vessel configuration and mini vessel configuration (left) and in more detail the mini vessel configuration of the setup (right). Source Pharma Test Apparatebau AG

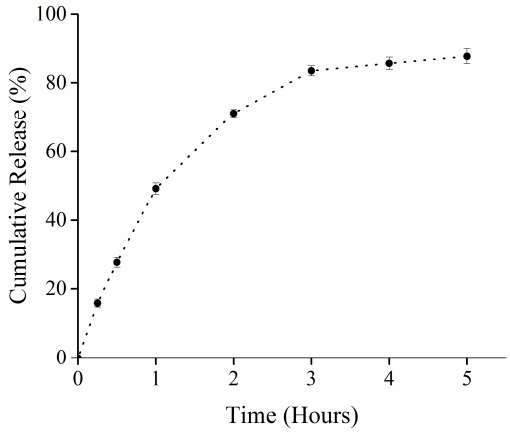

Figure 2. Cumulative drug release of drug-loaded polymer nanoparticles determined with the dispersion releaser technology at a molecular weight cut-off of 50 kDa (n=3).

A paddle stirring device inside the donor chamber ensures a rapid transport of the free drug through the dialysis membrane into the acceptor compartment where the drug concentration is quantified. The dissolution vessel is agitated by a magnetic stirring device at the same rate as the donor compartment.

The high sensitivity of the method is also indicated by the small standard deviation observed in the release experiments (see figure 2).

CONCLUSION

The DR technology allows a sensitive measurement of the drug-release from micro- and nanosized carriers. It uses the harmonized equipment described by USP, EP and JP and allows a highly reproducible and robust quantification of this parameter.

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