Practical Considerations When Using Fiber Optics for Dissolution Testing

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Introduction

The UV fiber optics system has emerged in dissolution testing of solid dosage forms as a useful alternative to conventional dissolution tests in both research & development and quality control. The system allows continuous in situ analysis of the drug concentration without the need for sample withdrawal and preparation. Therefore, this technique not only facilitates automation, but also eliminates potential errors in sample preparation. However, the fiber optic analysis itself possesses some sources of error. Several critical parameters, such as interferences with insoluble excipients and changes in hydrodynamics in the dissolution vessel with probe position have been thoroughly addressed by C. Schatz et al. [1].

In the first part of this study, the influence of the orientation of one-sided immersion probes (see figure 1) in the vessel was investigated. Stronger light scattering interferences on the dissolution results could be expected when the open side of the probe faces the flow direction, because the likelihood of insoluble excipients flowing into the light pathway is greater. In the second part of this study, interferences from air bubbles adhering to the immersion probe were evaluated. Without media deaeration, air bubbles might be formed during a dissolution test or while dipping the probe in the media.

A prednisolone 5-mg tablet formulation with a low drug to excipient ratio (drug content <4% m/m) was chosen for these studies.

Materials and Methods

Materials

Commercially available 5-mg Prednisolone tablets (Galenpharma GmbH Kiel, Germany, Lot 01362) were used for this study. Prednisolone refer-ence standard was purchased from Caelo Hilden, Germany (Lot 43772494). All other chemicals were analytical grade and purchased commercially.

Dissolution tests

A Varian IO fiber optic dissolution system was used for all dissolution studies. The system, consisting of a USP II VanKel 7020 dissolution tester and a Cary 50 photometer, combined with a Cassini multiplexer and fiber optic probes, was provided by Varian (Walnut Creek, CA, USA) and C-Technologies (Cedar Knolls, NJ, USA). The system was controlled by Cary WinUV Fiber Dissolution application soft-ware, which was configured to measure the drug absorption at 246 nm with a matrix compensation at 401 nm.

The dissolution studies were performed according to the USP 26 monograph "Prednisolone Tablets" [2], with n=6.

Profile accuracy

Parallel to the fiber optic analysis, manual samples were withdrawn and analyzed off-line using a V3000 spectrophotometer (Hitachi, Japan). The samples were withdrawn using a Fortuna Optima glass syringe (Fischer Labortechnik, Frankfurt/Main, Germany) fitted with a stainless steel cannula. The tip of the cannula was fitted with a 10-μm frit to prevent undissolved material from being withdrawn from the vessel. The sampling location in the dissolution vessel conformed to USP 26 guidelines [2]. The dissolution profiles from the two methods were compared using the f_2 test [3]. Note, that the f_2-test was applied to the entire dissolution profile and, for this and other reasons, did not conform to standard FDA f_2-test criteria (n=12, <20% coefficient of variation at earlier time points, maximum one time point with >85% dissolution) [4]. The parameters of the dissolution test are shown in Table 1.

Probe position study

Fiber optic dissolution tests were performed with three different, fixed probe positions (see Figure 2) and random positioning of the probes. The dissolution profiles were compared by calcu-

Figure 1: One-sided immersion probe (C-Technologies)

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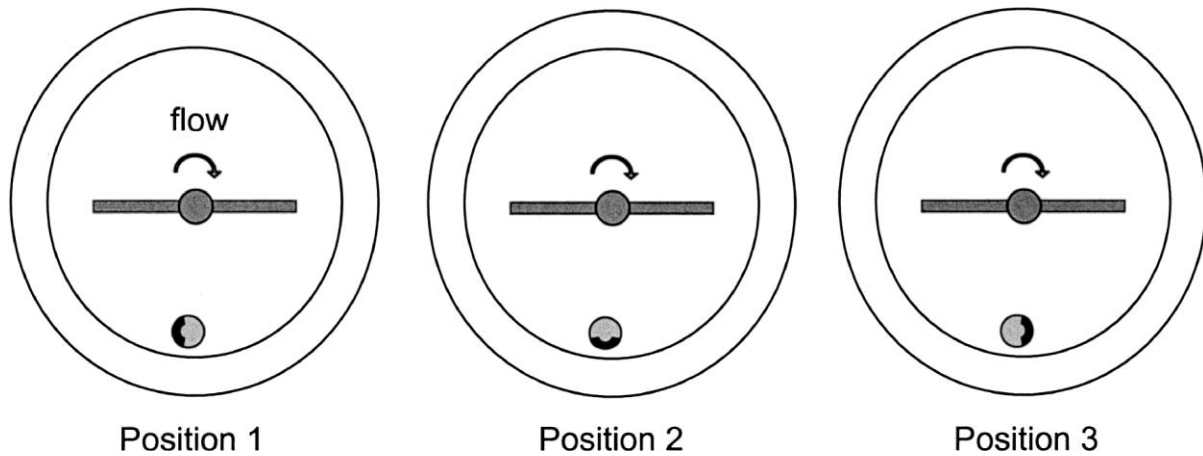# Practical Considerations When Using Fiber Optics ... *continued*

Figure 2: Varying immersion probe orientations in the dissolution vessel (top view)

Table 1: Dissolution test parameters

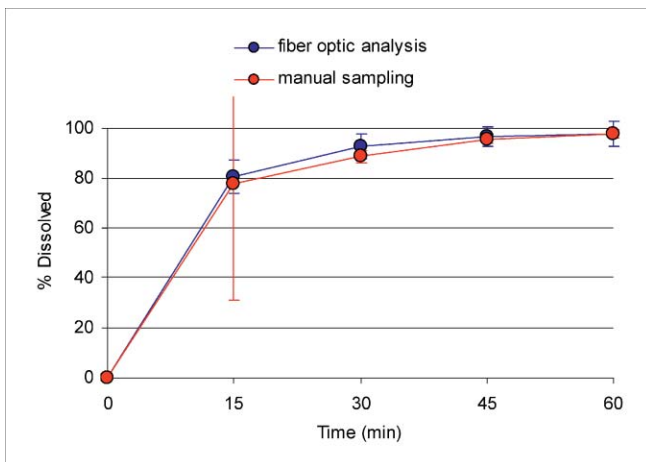| Test	Media and volume	Speed	Test duration	Sampling interval	Path length
Profile accuracy	Deaerated water 900 ml	50 rpm	60 min	15 min	10 mm
Probe position study	Deaerated water 900 ml	50 rpm	60 min	15 min	10 mm
Air bubble interference study	Untreated water 900 ml	50 rpm	60 min	5 min	10 mm
	Deaerated water 900 ml	50 rpm	60 min	5 min	10 mm

Figure 3: Dissolution profile of 5-mg Prednisolone tablets in water: fiber optic analysis versus manual sampling (n=6, ± SD)
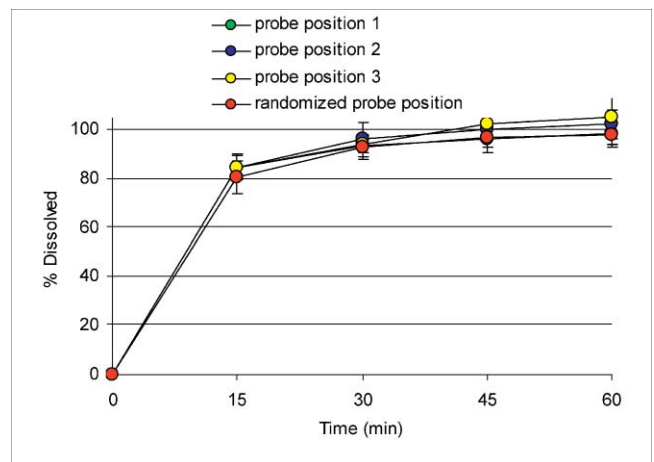

Figure 4: Influence of the probe orientation on the dissolution profile of 5-mg Prednisolone tablets (n=6, ± SD)

Table 2: F_2 values for the profiles obtained with probe positions 1, 2 and 3 compared to random probe position

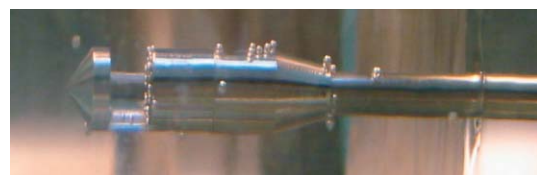| Probe position:	Position 1	Position 2	Position 3
f_2 value:	84	71	65

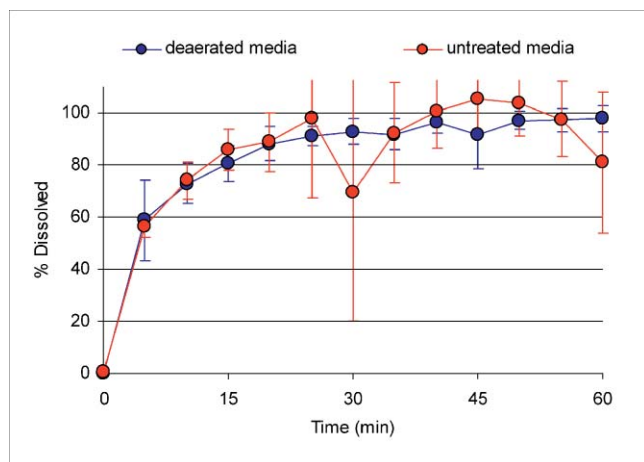*Figure 5: Air bubbles adhering to the immersion probe in untreated media*

Figure 6: Fiber optic analysis of 5-mg Prednisolone tablets in deaerated versus untreated media (n=6, ± SD)

lating the f_2 value (see above). Dissolution test parameters are displayed in Table 1.

Study of interference by air bubbles

In this study, two dissolution tests of identical design were performed with fiber optics, in deaerated media and in untreated media, to evaluate the influence on the dissolution profile of air bubbles formed on the probes. The dissolution test parameters are shown in Table 1.

Results
Accuracy of the fiber optic method

The results of the profile accuracy study are illustrated in Figure 3. Fiber optic and off-line analysis lead to comparable results. The calculated f_2 value is 78.

Influence of the probe position on fiber optic analysis

Various probe positions were used to determine whether differences in probe orientation would affect the dissolution process. No obvious change in the concentration/time profile was observed (Figure 4). A statistical comparison of the dissolution profiles with the f_2 test did not show any significant differences between the profiles (see Table 2).

Based on these results, it can be concluded that the probe orientation in the vessel plays at most a minor role in the fiber optic analysis.

Influence of air bubbles on the fiber optic analysis

For this study, the formation of air bubbles was evaluated by comparing dissolution profiles in deaerated and untreated media. Throughout the dissolution test in untreated media, the formation of air bubbles on the immersion probes was observed (see Figure 5). Figure 6 shows the mean dissolution profiles in deaerated and untreated media. The air bubbles lead to serious interferences in the fiber optic analysis, as can be seen by the erratic profile and the much higher standard deviations in the concentration/time values of the untreated media profile. The average coefficient of variation was 8.4% for the dissolution in deaerated versus 20.8% for the dissolution in untreated media.

Conclusion

Two practical concerns associated with the use of fiber optics in dissolution testing are the positioning of the probe and the influence of air bubbles on the results. This study demonstrated clearly that the orientation of the probe in the vessel has little or no effect on the profile, whereas air bubbles lead to undesirable variability in the data. The latter problem is effectively addressed by properly degassing the media.

Acknowledgements

References

1. Schatz, C., et al., Thoughts on fiber optics in dissolution testing, *Dissolution Technologies*, 2001. **8**(2): p. 6-11.
2. *USP 26 - NF 21*, ed. U.S.P. Convention. 2003, 12601 Twinbrook Parkway, Rockville, Maryland 20852, USA.
3. Moore, J.W. and H.H. Flanner, Mathematical comparison of dissolution profiles. *Pharmaceutical Technology*, 1996. **20**(6): p. 64-74.
4. Dissolution testing of immediate release solid oral dosage forms. FDA Guidance for industry, 1997.