dx.doi.org/10.14227/DT040197P16

Considerations in Choosing a Deaeration Technique for Dissolution Media

M.F. Griffith, T.E. Curley, and G.P. Martin
Merck & Co. West Point, PA

Abstract

Selection of a technique for deaeration of dissolution media will involve evaluation of several parameters, including effectiveness, cost and ease of use. When deciding to purchase a particular piece of laboratory equipment for dissolution deaeration, one needs a means to judge the effectiveness of the equipment. In this case, it was necessary to demonstrate the effectiveness of deaeration (1,2). The USP method was used as a benchmark and other deaeration techniques were compared to this method. Various deaeration techniques (involving different degrees of complexity and expense) were found to be comparable to the USP method of deaeration (3,4). After determining deaeration effectiveness, one can then choose a method based on individual laboratory needs, e.g., budget, manpower.

Introduction

Dissolution results for some pharmaceutical dosage forms may be affected by dissolved air in the dissolution medium. This effect can be eliminated by effective deaeration of the dissolution medium. Parameters chosen to judge the effectiveness of deaeration have typically been dissolved oxygen content and results from calibrator tablets. A dissolution calibration method known to be sensitive to deaeration , the NCDA #2 tablet method, (5) was chosen to determine efficacy of deaeration. The USP calibrator tablet method was not chosen because of known insensitivity to deaeration using prednisone tablets at 50 rpm with Apparatus 2(6). Other parameters involved in the selection of a deaeration method are ease of use and expense. For the evaluation of the different deaeration techniques, the USP method was chosen as the benchmark (2). The effectiveness of the dearation techniques was evaluated by measuring the amount of dissolved oxygen in the deaerated dissolution media and evaluating the results from the dissolution of the NCDA #2 test performance tablets.

Experimental

1. A YSI model 5004 Dissolved Oxygen Meter was used to measure the dissolved oxygen content of the deaerated dissolution media. The instrument was calibrated daily according to the manufacturer's directions.

2. The method and specifications for the NCDA #2 test performance tablets was followed (5).

3. Preparation of dissolution media: deionized water was used in the evaluations.

4. Deaeration Techniques:

   a. None

   b. USP technique: Heat the medium, while stirring gently, to about 45°C, immediately filter under vacuum using a filter having a porosity of 0.45 µm or less, with vigorous stirring, and continue stirring under vacuum for about 5 minutes

   c. Membrane Degassing: a commercial device which utilizes a deaeration technique by pulling a vacuum across a semi-permeable membrane (7).

   d. Helium sparging: Helium was bubbled through the medium via an HPLC solvent inlet filter at a rate of about 50 mL/minute. Sparging was done for 30 minutes.

Results

Results for the dissolved oxygen determination *(Table 1)* showed significant reduction in dissolved oxygen content for all of the techniques when compared to no deaeration. Results showed no significant differences among the 3 deaeration techniques. The NCDA #2 test *(Table 2)* showed results which were significantly lower when the medium was deaerated than when there was no deaeration, and results were within the acceptable range when using each of the deaeration techniques. No significant differences were seen among the results for the 3 deaeration techniques.

Table 1. % Dissolved Oxygen Found after Deaeration

Deaeration Technique	Dissolved Oxygen mg/L
None (n=6)	13.0
USP (n=6)	4.8
Membrane Degassing (n=6)	5.6
Helium sparging 30 minutes (n=6)	5.2

Other Considerations:

The USP technique and helium sparging are relatively inexpensive. The USP technique requires stir bars, a hot plate/stir plate and a means to draw vacuum. Helium

Table 2: Comparison of Deaeration Techniques for Prednisone 10 mg NCDA Test Performance Standard #2

Deaeration Technique	% Dissolved (n=12)	RSD (%)
None (n = 6)	50**	11
USP technique	35	11
Membrane Degassing	36	11
Helium Sparging 30 minutes	36	8

** fails acceptance limits
Acceptance Limits: Range of 30%-50% of label for individual tablets and a range of 35%-43% for the mean of 6 tablets (5).

sparging requires a manifold to deliver helium; it can be difficult to consistently control helium flow. Both the USP technique and helium sparging can require manipulation of large amounts of media. The media must be poured volumetrically into individual pots and the media must come to temperature before dissolution testing can begin. On the issue of timeliness: both USP and the helium sparging method of deaeration require at least 45 minutes of human intervention. Neither the USP or helium sparging method offers ease of dissolution media handling. The membrane degassing device fills vessels with the required amount of deaerated medium at the preset temperature. Media is not required to be poured and when the vessels are filled the temperature is 37° ±0.5°C. The membrane degassing device (Erweka Dissofill) was chosen as the preferred method of deaeration since it offers timeliness as well as ease in handling dissolution media *(Table 3)*.

Table 3: Comparison of Considerations for Deaeration Techniques

Technique	Cost	Preparation Time
USP	$510	45 min/6 pots
Helium Sparging	$1300/year **	45 min/6 pots
Membrane Degassing	$8800	10 min/6 pots

** Estimate based on 10% of the current helium usage for our department. Assumes the presence of helium equipment for other uses.

Conclusions

This lab demonstrated that the 3 deaeration techniques are equivalent. Other techniques could be evaluated using the same or similar criteria. The selection of a deaeration technique will depend on several factors: frequency of dissolution testing, amount of dissolution testing, source of manpower and other individual needs. In this lab, many dissolutions are handled on a daily basis; there is need for consistency among a large number of users, ease of handling, and timeliness. For this lab, the membrane degassing deaeration device was chosen.

References

1. *Hanson, W.A., Handbook of Dissolution Testing, 2nd Edition, Revised, Aster Publishing Corporation, Eugene, Oregon, 1991.*

2. *Gray, V.A., Hubert, B.B., Calibration of Dissolution Apparatuses 1 and 2 What To Do When Your Equipment Fails. Pharm. Forum, 20:6 (1994) 8571-8573.*

3. *Qureshi, S.A., McGilveray, I.J., Impact of Different Deaeration Methods on the USP Dissolution Apparatus Suitability Test Criteria. Pharm. Forum, 20:6 (1994) 8565-8566.*

4. *Rohrs, B.R., Stelzer, D.J., Deaeration Techniques For Dissolution Media. Dissolution Technologies, 2:2, (1995) 1,7-8.*

5. *Moore, T.W., Shangraw, R.F., Habib, Y., Dissolution Calibrator Tablets: A Recommendation for New Calibrator Tablets to Replace Both Current USP Calibrator Tablets. Pharm Forum, 22:3 (1996) 2423-2428.*

6. *Moore, T.W., Hamilton, J.F., Kerner, C.M., Dissolution Testing: Limitations of the USP Prednisone and Salicylic Acid Calibrator Tablets. Pharm Forum, 21:5 (1995) 1387-1398.*

7. *Dissofill Automated Media Preparation Device , Erweka Instruments, Inc. Milford, CT*