Considerations in Choosing a Deaeration Technique for Dissolution Media

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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 deaeration 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. Ddeaeration 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.

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
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°C ±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 2: Comparison of Deaeration Techniques for Prednisone 10 mg NCDA Test Performance Standard #2

<table>
<thead>
<tr>
<th>Deaeration Technique</th>
<th>% Dissolved (n=12)</th>
<th>RSD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None (n = 6)</td>
<td>50**</td>
<td>11</td>
</tr>
<tr>
<td>USP technique</td>
<td>35</td>
<td>11</td>
</tr>
<tr>
<td>Membrane Degassing</td>
<td>36</td>
<td>11</td>
</tr>
<tr>
<td>Helium Sparging</td>
<td>36</td>
<td>8</td>
</tr>
<tr>
<td>30 minutes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

** ** 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).

### Table 3: Comparison of Considerations for Deaeration Techniques

<table>
<thead>
<tr>
<th>Technique</th>
<th>Cost</th>
<th>Preparation Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>USP</td>
<td>$510</td>
<td>45 min/6 pots</td>
</tr>
<tr>
<td>Helium</td>
<td>$1300/year</td>
<td>45 min/6 pots</td>
</tr>
<tr>
<td>Sparging **</td>
<td></td>
<td>10 min/6 pots</td>
</tr>
<tr>
<td>Membrane Degassing</td>
<td>$8800</td>
<td></td>
</tr>
</tbody>
</table>

** ** 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 dissolution tests 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

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