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## Back to Basics: Dissolution Testing 1: Apparatus Overview

G. Bryan Crist1 and R. B. Walker2

This is the third in a series of articles introducing the basics of aspects of research techniques that may be required for the development and evaluation of controlled release technologies.

## Introduction

This is the first in a series of articles on dissolution testing and covers basic operational information for the appropriate execution of dissolution testing to ensure reproducibility and/or reliability. Furthermore, several tips for keeping apparatus in top operating condition are provided.

Our primary intention is to provide a "back to basics" approach for conducting dissolution tests, since many analysts learn how to operate dissolution apparatus from other analysts. While the intention is that the trainer imparts only "good habits," in reality several "short-cuts" are often imparted. Any deviation or misinterpretation of the compendial requirements for a dissolution test may result in bias or variability of test results and, thus, must be avoided. We are not necessarily saying that bad habits are learned, but rather that occasionally an incorrect interpretation of the requirements of the USP or other official compendium takes place. For example, an analyst may not see the need to de-aerate the dissolution media, since many monographs contained in the USP describe the preparation of dissolution medium without this essential step. However, the physical test chapter on dissolution states, "Dissolved gases can cause bubbles to form, which may change the results of the test. If dissolved gases influence the dissolution results, dissolved gases should be removed prior to testing" (1).

The effects of de-aeration should be documented during the validation of a dissolution method to evaluate bias in test results caused by the presence of air bubbles on the surface of the vessel and/or shaft. The presence of bubbles generally causes more turbulence in the vessel, which can lead to an increase in the dissolution rate of an active compound. If an analyst tests a disintegrating dosage form without proper de-aeration of the medium, a faster release rate could be observed. This could result in the release of a sub-performance batch of tablets from the quality control laboratory, which is responsible for detecting performance issues through the conduct of a properly validated dissolution test.

Prior to discussing dissolution testing apparatus in detail, it is appropriate to provide an overview of the environment in which that apparatus is located and maintained (Figure 1).

At the outset, the apparatus should be placed on benches with sturdy construction and located some distance away from any sources of vibration, such as fume hoods, centrifuges, tapped density test instruments, vacuum pumps, ultrasonic baths, shaker apparatus, and mixers. Bench tops constructed of very dense material transmit vibrations over long distances, and therefore, long sections of benches should be constructed with gaps located at suitable intervals. For example, it should not be assumed that an ultrasonic bath located a meter away from a dissolution apparatus will not be used while a dissolution test is in progress. The primary purpose of an ultrasonic bath in a laboratory is to dissolve solids; if it is used during dissolution testing, it may have an adverse effect on the dissolution test.



Figure 1. Preparing for a dissolution test.

The Dissolution Environment

<sup>1</sup> Scientific Affairs Manager-Pharma, Varian, Inc., Cary, NC, U.S.A.

<sup>&</sup>lt;sup>2</sup> Head and Dean, Faculty of Pharmacy, Rhodes University, Grahamstown, South Africa.



Figure 2. Filtration of the dissolution sample.

should be placed away from benches that are connected to walls supporting heavy doors or located on the other side of stairways. As doors slam, particles located in an apparatus basket can sift out during a dissolution test. This introduces variability and may alter test results. All potential sources of vibration present outside the immediate laboratory environment must also be evaluated. Many analytical laboratories are located in

Dissolution apparatus

close proximity to pharmaceutical manufacturing and processing equipment or high-traffic areas where product and materials are transported. In short, if you would not place an analytical balance in a location due to vibration, you should not locate dissolution test apparatus at that site.

Many laboratories have limited space available for both dissolution apparatus and peripheral equipment. The laboratory should have ample space for preparing test media without affecting the dissolution test apparatus while tests are being conducted. It is recommended that the lab have a test medium preparation station with a large volume source of purified water. The preparation of large volumes of dissolution medium may require the use of mixers, de-aeration equipment, measuring and dispensing equipment, and water baths to preheat test media. In terms of occupational safety, equipment must be available to assist analysts with moving carboy containers holding more than 25 L of media. In addition, the floors in the laboratory should be coated with a non-slip material, since liquid is routinely spilled when removing and cleaning dissolution vessels or when transferring media from the preparation area to test areas.

## The Dissolution Apparatus

A dissolution test usually consists of two steps: sample preparation and analysis. A validated filtration step usually separates the sample preparation and analysis procedures (Figure 2). The filtration step must demonstrate the cessation of dissolution following the removal of un-dissolved particles and the clarification of the sample prior to analysis.

Occasionally dissolution apparatus are referred to as dissolution testers despite the fact that they do not test anything but are rather instruments used for sample preparation under precisely controlled conditions. Sample preparation commences upon the introduction of the dosage form, usually a solid oral dosage form, into the basic dissolution environment. This environment is quite simple and consists of three primary components: the vessel, the media, and an agitation element.

The dissolution environment is a simple symmetrical environment that should minimize and avoid the introduction of additional turbulence during the test. Therefore, the equipment must maintain proper agitation shaft and vessel alignment, agitation speed, and media temperature. Apparatus should be constructed to minimize the effects of vibration from internal components or external sources.

Dissolution apparatus are available from manufacturers worldwide. The apparatus should be capable of passing established performance-testing criteria outlined by compendial and regulatory agencies to ensure the accurate and precise data necessary to evaluate the performance of pharmaceutical dosage forms. Without precise control of the dissolution environment, factors such as increased turbulence may contribute to faster dissolution rates, increasing the possibility of incorrect formulation characterization during research and development or the release of sub-performing lots for distribution.

In addition to strong apparatus design and construction, routine evaluation and maintenance ensure conformance to the critical tolerances and specifications outlined by the appropriate pharmacopeia (Figure 3). Prior to use, the apparatus must be

properly qualified and subjected to installation (IQ), operation (OQ), and performance (PQ) qualification procedures. Once qualified, the apparatus should not be moved or disturbed in its location.



Figure 3. Checking physical parameters prior to the dissolution test.

Required qualification

procedures for a dissolution apparatus and its associated operation will follow in subsequent newsletter articles. In addition, topics will cover aspects of intrinsic dissolution, novel dosage form testing, compendial drug release testing apparatus, and analyst training.

It has been said that a dissolution apparatus may be compared to a finely tuned, precisely crafted violin made with the finest materials. If the violin is not played by an experienced musician, it will not make music. Similarly, no matter how well made, calibrated, and maintained a dissolution apparatus is, it must be used by an analyst who has a thorough knowledge of all aspects of dissolution testing to produce appropriate results.

## Reference

1. Dissolution, U.S. Pharmacopeia, USP 32, NF 27, Vol. 1, <711> p. 268 (2009). ■