

Drug Dissolution Testing

Basic Principles & Practices

By

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Biographical Sketch of Dr. Qureshi



Dr. Qureshi has extensive (30+ year) experience in conducting hands-on and multi-disciplinary laboratory research in pharmaceutical areas for regulatory assessment purposes while working with Health Canada.

He is an internationally recognised expert in the areas of pharmacokinetics, biopharmaceutics, drug dissolution testing, analytical chemistry as related to characterization of pharmaceuticals, in particular based on in vitro (dissolution) and bioavailability/bioequivalence (humans and animals) assessments.

At present, Dr. Qureshi provides teaching, training and consulting services, in the area of his expertise as noted above, for improved pharmaceutical products development and assessments. Dr. Qureshi can be reached by email (principal@pharmacomechanics.com) or Tel (+1 613 797 9815)

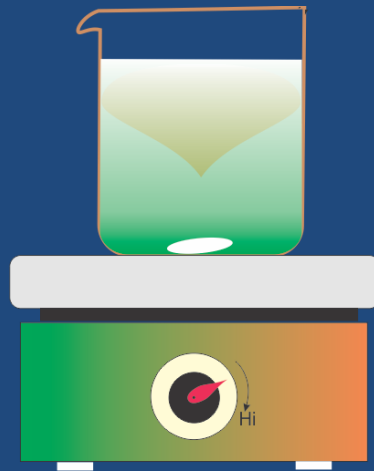
Outline:

- **What is dissolution testing?**
- **Why is the testing needed?**
- **How is it conducted?**
- **Deficiencies & suggested improvements**

What is dissolution testing? ... 1

It is a technique used for measuring the rate of drug release from a product (such as tablet or capsule) into a solvent.

What is dissolution testing? ... 2



For all practical purposes it is a modified, or refined, method of observing solubility of a drug in a *solvent* in a “beaker” with a *stirrer*.

Why do we need dissolution testing?

- To study the release characteristics of a drug from the product such as tablet and capsule in humans.
- The testing, or its requirement, is based on the fact that, when administered through oral route, the drug must be absorbed from the GI tract, and for the absorption the drug should be in solution form, thus assessment of dissolution characteristics.

How to conduct a dissolution test?

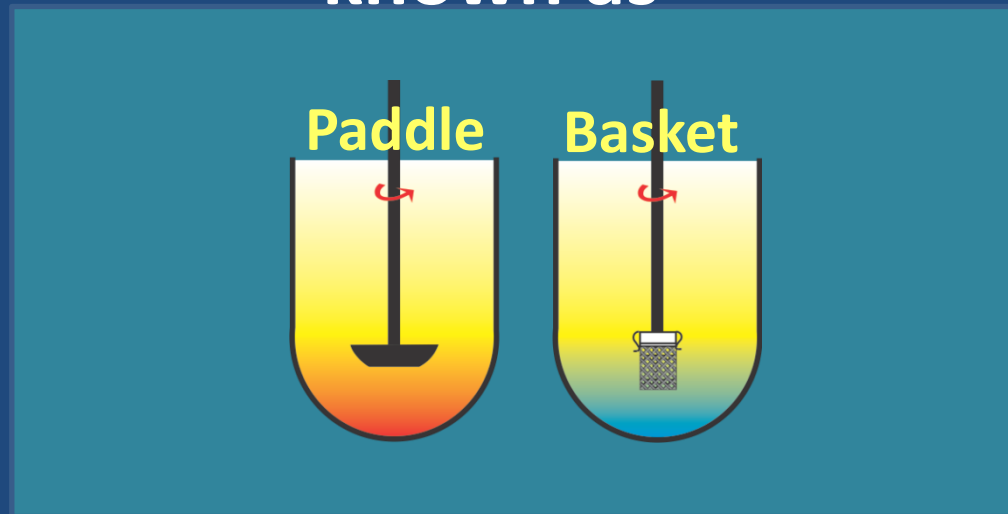
- The objective of the test is to measure drug dissolution characteristics in humans, in particular GI tract, therefore experimental conditions must reflect GI tract environment.
- It is important to note that one needs to simulate environment not to duplicate the physiology or anatomy of the GI tract.
- In this regard, two conditions need to be met: (1) nature of the solvent including its pH and temperature, and (2) stirring and mixing environment.

Commonly recommended experimental conditions - 1

Solvent: 900 mL of 0.1 or 0.01N HCl, water or buffer having pH in the range of 4.5 to 7 maintained at 37 °C as per pharmacopeias e.g. USP.

Commonly recommended experimental conditions - 2

Specialized beakers and stirrers known as -



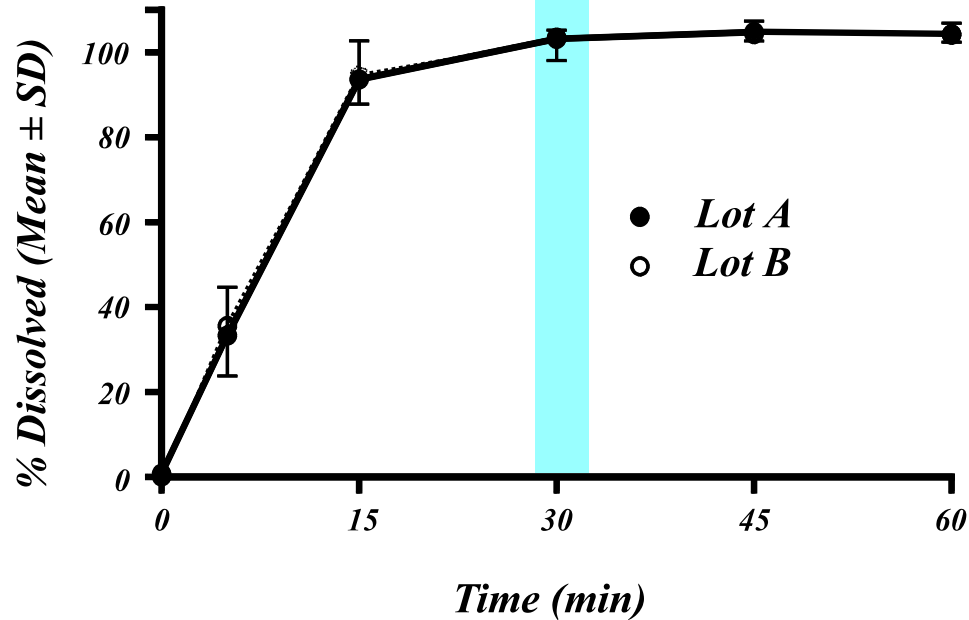
*With rotation speed between 50 to 100 rpm
– as per pharmacopeias e.g. USP*

Commonly recommended experimental conditions - 3

A typical dissolution tester



Reporting of dissolution results



Source: Qureshi & McGilveray, *Pharmacoepial Forum*, (1991), p. 1973

Commonly recommended experimental conditions - 4

In short, a typical dissolution test is conducted by dropping a tablet/capsule into a round bottom vessel containing 900 mL of solvent maintained at 37 °C with stirrer (paddle/basket) set at usually 50 rpm. After a specified time period(s) which ranges from 15 minutes to several hours (depending on product) a sample, or samples, is withdrawn to measure the amount of drug in solution which establishes the dissolution characteristics of the product.

Commonly recommended experimental conditions – 4 (*Repeat*)

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Issues with current practices of dissolution testing - 1

- Numerous!
- However, these issues can be divided in two broad categories

Issues with current practices of dissolution testing - 2

- Use of non-validated testers i.e. testers (paddle/basket) have never been shown to be capable of providing relevant and reproducible dissolution results.
- Use of experimental conditions which are not physiologically relevant.

Issues with current practices of dissolution testing - 3



This picture is taken from a video clip of a dissolution test, demonstrating lack of stirring and mixing within dissolution vessels/apparatuses, essential for appropriate dissolution testing. Thus, it is not possible to obtain appropriate dissolution characteristics of a product.

Issues with current practices of dissolution testing - 4

- Commonly recommended (e.g. USP) dissolution tests are drug and/or product dependent. However, as a dissolution test is to be conducted to reflect dissolution characteristics in the GI tract where environment remains consistent (or drug/product independent), the drug and/or product dependent dissolution tests become physiologically irrelevant.
- As the currently recommended tests are drug/product dependent, therefore, it is also not possible to determine unbiased dissolution characteristics of the products or to make valid comparison between products.

Suggestion for addressing the issues and improving the dissolution testing -1

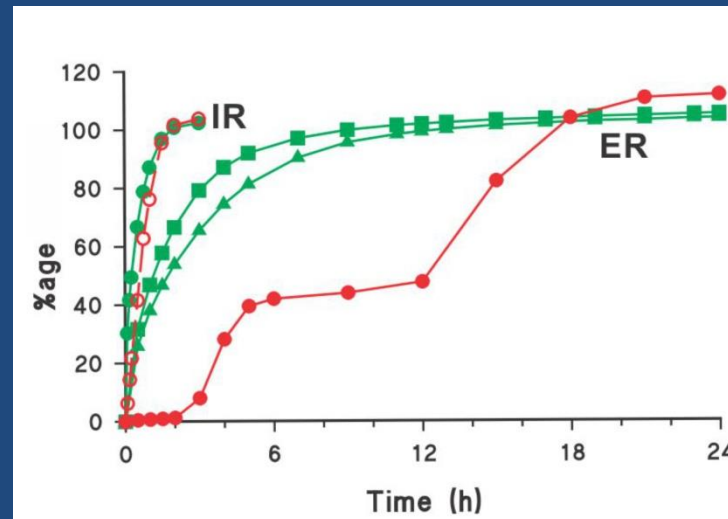


A new stirrer, known as Crescent-shape spindle, has been suggested. The stirrer (spindle) sits at the base the vessels and provides efficient stirring and mixing even at lower rotation speed of 25 rpm.

Suggestion for addressing the issues and improving the dissolution testing -2

- As the stirring and mixing problem is resolved, a universal (drug/product independent) dissolution test/tester becomes a possibility. The suggested dissolution test/tester would be: 900 mL of water maintained at 37 °C using the Crescent-shape spindle set at 25 rpm. Low solubility drugs may require addition of some solubilizer (e.g. sodium lauryl sulphate) to facilitate complete solubilization of the drug in water for its appropriate quantitation.
- As the suggested test is drug/product independent, thus becomes physiologically relevant consistent with common or product independent GI tract environment.

Suggestion for addressing the issues and improving the dissolution testing -3



- Dissolution profiles of (diltiazem and carbamazepine) products using suggested common/universal experimental conditions.
- At present, such testing would require numerous methods (experimental conditions).

Summary and conclusions - 1

- Dissolution testing is a technique used for evaluating drug characteristics of products, in particular tablet and capsule, in humans.
- It is commonly used for the development of products and often a regulatory requirement to assess the quality of the products.
- At present, dissolution testing is commonly conducted using pharmacopeial apparatuses known as paddle and basket.
- These apparatuses, however, have never been validated for their intended purpose.

Summary and conclusions - 2

- In addition, because of poor stirring and mixing environment within vessels these testers do not provide relevant and consistent results. Thus appropriate dissolution testing and product evaluation is not possible.
- A modified stirrer, known as Crescent-shape spindle, has been suggested to address the current issues of the drug dissolution testing.
- The suggestion provides a simple and universal dissolution testing approach leading to improved and physiological relevant testing.

Thank you!

*For further information, please visit his blog
(www.drug-dissolution-testing.com) or contact Dr.*

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