Oral Solid Dosage Form Disintegration Testing — The Forgotten Test

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ABSTRACT: Since its inception in the 1930s, disintegration testing has become an important quality control (QC) test in pharmaceutical industry, and disintegration test procedures for various dosage forms have been described by the different pharmacopoeias, with harmonization among them still not quite complete. However, because of the fact that complete disintegration does not necessarily imply complete dissolution, much more research has been focused on dissolution rather than on disintegration testing. Nevertheless, owing to its simplicity, disintegration testing seems to be an attractive replacement to dissolution testing as recognized by the International Conference on Harmonization guidelines, in some cases. Therefore, with proper research being carried out to overcome the associated challenges, the full potential of disintegration testing could be tapped saving considerable efforts allocated to QC testing and quality assurance. © 2014 Wiley Periodicals, Inc. and the American Pharmacists Association J Pharm Sci 104:2664–2675, 2015

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INTRODUCTION

It is a well-known fact that an immediate-release dosage form should disintegrate in order to efficiently liberate its active ingredient(s) and make it available for absorption. Therefore, disintegration testing methods were developed.

The first mention of a test for disintegration was in the 1907 Edition of *Pharmacopoeia Helvetica*, in the compressed pastilles monograph, stating that they should dissolve or disintegrate after a short time of them being placed in cold water.[1] In 1933, a disintegration test for tablets appeared in the same pharmacopoeia.[2] It stated that a tablet should be placed in a 100-mL Erlenmeyer flask containing 50 mL of water, at a temperature of 37°C, and the flask was to be gently swirled from time to time.[2] It was stated that the tablet had to disintegrate into a powder or dissolve within 15 min.[2]

In 1948, the British Pharmacopoeia (BP) adopted a disintegration test for tablets based on observing the disintegration behavior in test tubes.[3] However, by that time, a specific disintegration testing apparatus had been used for 8 years by the laboratories of US Army Medical Department (Fig. 1),[4] and this apparatus formed the basis for the basket-rack assembly apparatus, first adopted by the United States Pharmacopoeia (USP) in 1950,[5] which is the apparatus currently used to perform the vast majority of disintegration testing procedures for orally administered dosage forms.

Since then, the disintegration test has been a major quality control (QC) test in pharmaceutical development and QC. However, it has been well understood that, despite disintegration being a prerequisite for acceptably rapid drug dissolution, complete disintegration does not necessarily imply complete dissolution of the active ingredient. This has contributed to the much greater focus on dissolution testing methods in pharmaceutical research, which can be easily noticed by the much greater amount of publications dealing with dissolution testing methodologies compared with those dealing with disintegration testing methodologies (as shown in Fig. 2).

Nevertheless, the greater simplicity of disintegration compared with dissolution testing (e.g., no analytics needed, lesser volume of fluids required, less time-consuming) makes the idea of putting more focus on disintegration attractive. This has been recognized by the International Conference on Harmonization (ICH) that allowed the use of disintegration testing as a surrogate for dissolution testing if certain conditions are met.[6] Therefore, focusing more interest and research on disintegration testing could, because of the test's simplicity, enable the QC departments of pharmaceutical companies to save appreciable expenses in terms of time, efforts, and even money.

In this commentary, disintegration testing is discussed and possible means of enhancing its potential as a QC method in the pharmaceutical industry are introduced. Particular focus will be given to its potential use as a surrogate for dissolution testing.

DISINTEGRATION APPARATUS

A disintegration apparatus is composed of a 1-L low-form cylindrical beaker, a heating system that keeps the temperature at 37 ± 2°C, a basket-rack assembly, and a device to move the basket-rack assembly vertically.[7–10] Two types of basket-rack assembly are described: apparatus A (Fig. 3) and apparatus B (Fig. 4). Apparatus A is described in all major pharmacopoeias: European Pharmacopoeia (Ph Eur), BP, USP, and Japanese Pharmacopoeia (JP), whereas apparatus B is described only in the Ph Eur, BP, and the Dietary Supplements chapter of the USP, where it is required for testing tablets and capsules more than 18 mm in length.[7–10] The chapters on disintegration testing are harmonized between Ph Eur and BP.

Both types consist of a set of open-ended transparent tubes maintained in a vertical position by two plates containing the corresponding number of openings arranged in a circle

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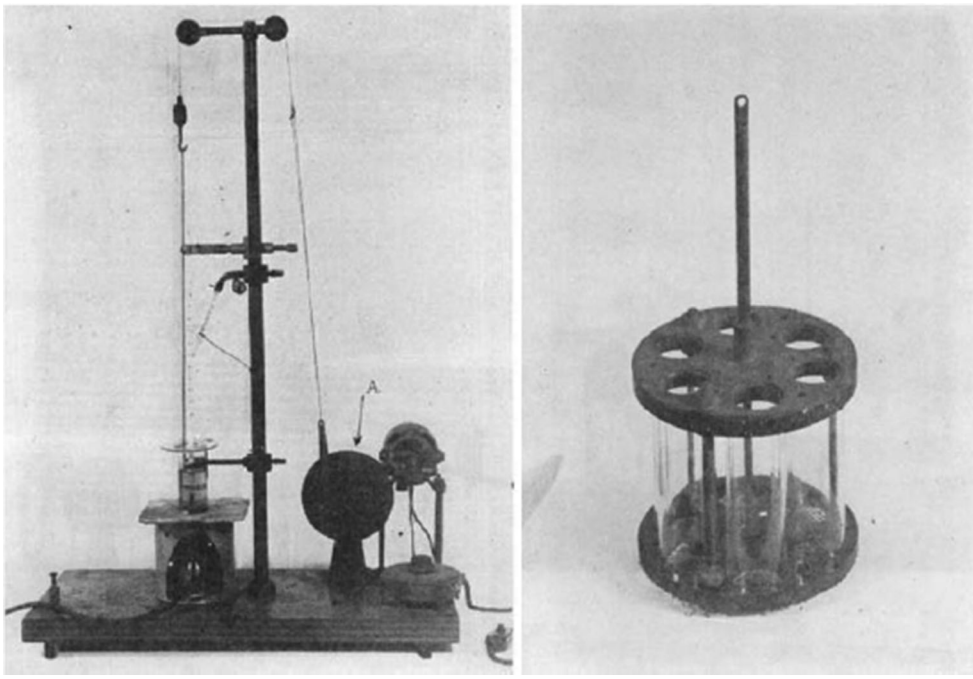

Figure 1. Disintegration apparatus from the 1940's before becoming official in the USP.[4]

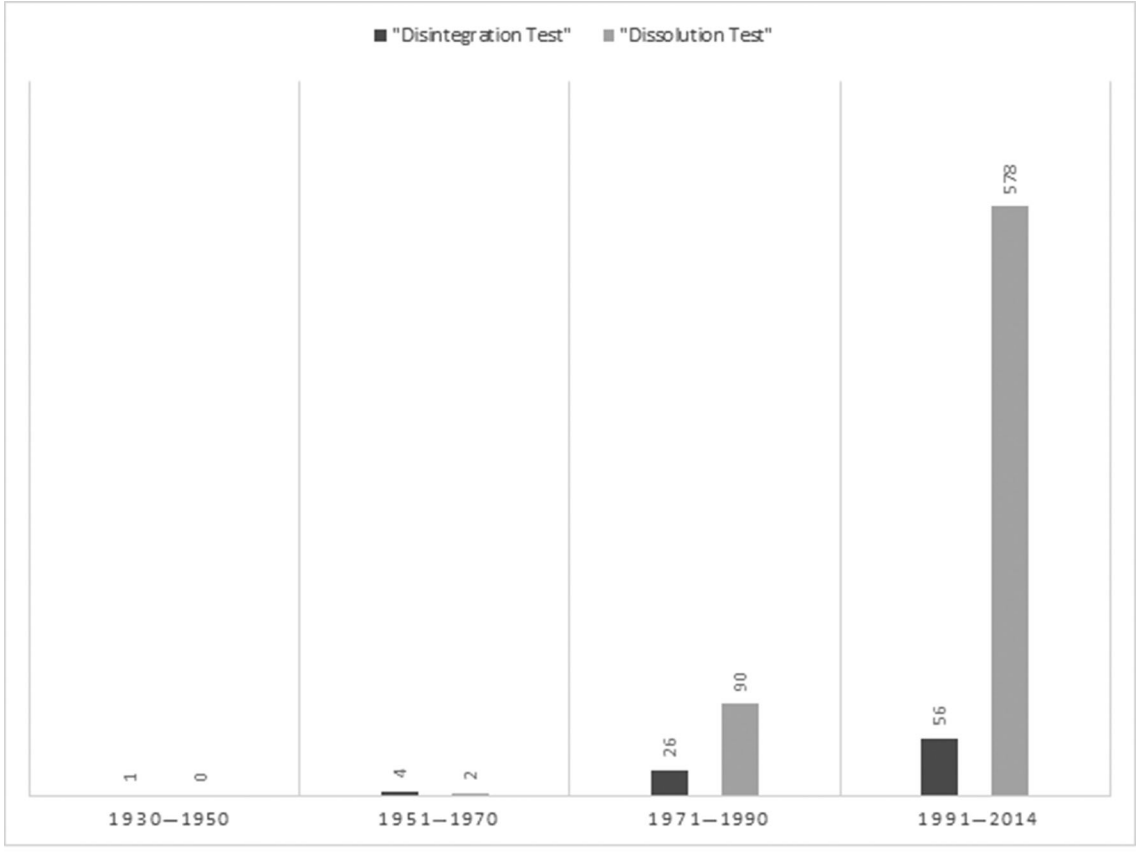

Figure 2. Hits when searching for the terms "Disintegration Test" and "Dissolution test" within the date ranges shown on the x-axis in PubMed. Accessed June 23, 2014.