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Review Article

A REVIEW ON DISSOLUTION APPARATUS

Shobhit Sharma*, M.P. Khinchi, Dilip Agrawal, Natasha Sharma, M.K. Gupta,

Department of Pharmaceutics, Kota College of Pharmacy, Kota, Rajasthan, India

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ABSTRACT

For orally administered non-solution dosage forms, in vitro performance test procedure such as dissolution test is performed for various purposes. It is one of the routinely performed quality control tests for the oral solid dosage forms. Dissolution research started to develop about 100 years ago as a field of physical chemistry and since then important progress has been made. Apart from its importance in the field of pharmaceutical analysis it is also important in pharmaceutical formulation technology and drug discovery. In this review paper we will focus on different mathematical aspects of dissolution process and different dissolution apparatuses are in use. We will discuss some non-conventional dissolution testing methods. The review will also focus on modernization of dissolution process and dissolution testing apparatuses including automation in dissolution testing and adoption of fiber optic technology.

Key Words: *Dissolution, Apparatus, Dissolution testing, pharmaceutical Formulation*

INTRODUCTION

Dissolution testing is an official test used by pharmacopeia for evaluating drug release of solid and semisolid dosage forms dissolution tests were first developed to quantify the amount and extent of drug release from solid oral dosage forms including immediate/sustained release tablets and capsules. More recently, dissolution has become important in testing drug release of dosage forms such as, buccal and sublingual tablets, chewing gums, soft gelatin capsules, suppositories, transdermal patches, aerosols and semisolids the study of the dissolution process has been developing since the end of the 19th century by physical chemists. The goal is to have a fully functional set of USP performance tests for all kinds of dosage forms.

**For Correspondence:*
Shobhit Sharma
Department of pharmaceutics,
Kota College of pharmacy, Kota
E.mail: shobhitsharma53@rediffmail.com
Mobile No: 09414967720

Solid dosage form (tablet and capsule):

I.P. and E.P.:

Apparatus I – paddle apparatus

Apparatus II – basket apparatus

B.P. and U.S.P.:

Apparatus I – basket apparatus

Apparatus II – paddle apparatus

B.P. and E.P:

Apparatus III – flow through cell apparatus

Conditions (for all):

Temp - 37±0.50C

PH - ±0.05 unit in specified monograph

Capacity – 1000 ml

Distance between inside bottom of vessel and paddle/basket is maintained at 25±2 mm. For enteric coated dosage

Form it is first dissolved in 0.1 N HCl and then in buffer of pH 6.8 to measure drug release. (Limit – NMT 10% of

Drug should dissolve in the acid after 2hr.and about 75% of it should dissolve in the buffer after 45 min.

USP apparatus are of 7 types they are as follows

Type 1 USP apparatus: (Basket apparatus)

- Dosage form contained within basket.
- Dissolution should occur within Basket.
- pH change by media exchange.

Useful for: Tablets, Capsules, Beads, and Floaters

Type 2 USP apparatus: (Paddle apparatus):

- Dosage form should remain at the bottom centre of the vessel
- Sinkers used for floaters
- pH change by media addition

Useful for: Tablets, Capsules

Type 3 USP apparatus: (Reciprocating cylinder):

- Rotations 6-35 rpm

Useful for: Tablets, Beads, controlled release formulations

Type 4 USP apparatus: (Flow through cell apparatus):

Useful for: Low solubility drugs , Rapid degradation , Media PH change

Type 5 USP apparatus: (paddle over disk)

- Rotations 25-50rpm

Useful for: Transdermal patches, Ointments, Floaters, Emulsions, Bolus

Type 6 USP apparatus: (Cylinder apparatus):

Useful for: Transdermal patches

Type 7 USP apparatus: (Reciprocating holder):

- Rotations 30rpm

Useful for: Transdermal patches, Solid dosage forms, pH profile, Small volumes.

USP apparatus 4 and apparatus7 and modifications of the official apparatuses have shown great potential and

Value for in vitro release for novel dosage forms. [1, 2]

DIFFERENT DISSOLUTION TESTING APPARATUS

The USP has 7 different apparatus that can be used for dissolution testing although most tablets and capsules use Apparatus 1 or 2 also known as basket and paddle. These two apparatus were developed through the 1960s and adopted by the USP in the 1970s. [3]

• USP Apparatus 1 (Basket Apparatus)

The basket method was first described in 1968 by Pernarowski and his co-workers. [4] The most commonly used methods for evaluating dissolution first appeared in the 13th edition of the U.S. Pharmacopeia in early 1970. These methods are known as the USP basket (method I) and paddle (method II) methods and are referred to as "closed-system" methods because a fixed volume of dissolution medium is used. [5] In practice a rotating basket method provides a steady stirring motion in a large vessel with 500 to 1000 mL of fluid that is immersed in a temperature –controlled water bath. Basket method is very simple, robust, and easily standardized. The USP basket method is the method of choice for dissolution testing of immediate-release oral solid dosage forms. [6]

This apparatus is useful for tablets, capsules, beads and floaters. Solids (mostly floating), monodisperse (tablets) and polydisperse (encapsulated beads) drug products are commonly tested using USP Apparatus 1 (Figure 1). An apparatus described by Levy and Hayes [7] may be considered the forerunner of the beaker method. It consisted of a400 ml beaker and a three-blade, centrally placed polyethylene stirrer (5 cm diameter) rotated at 59 rpm in 250 ml of dissolution fluid (0.1N HCl). The tablet was placed down the side of the beaker and samples were removed periodically. In the Apparatus 2, (the paddle apparatus method) a paddle replaces the basket as the source of agitation. As with the basket apparatus, the shaft should position no more than 2mm at any point from the vertical axis of the vessel and rotate without significant wobble. [8] The apparatus is useful for tablets, capsules and suspensions.

Like USP Apparatus 1 solids (mostly floating), mono disperse (tablets) and poly disperse (encapsulated beads) drug products are commonly tested using USP Apparatus 2. But floating dosage forms require sinker which could be considered as a disadvantage of the apparatus. Moreover cone formation and positioning of tablet during the test is sometimes hard to maintain. [9] Both the USP Apparatus 1 and 2 share some common advantages and disadvantages.

Advantages include:

- Widely accepted apparatus for dissolution test,
- Apparatus of first choice for solid
- Figure 1. Schematic diagram of (A) USP Apparatus 1 and (B) USP Apparatus 2

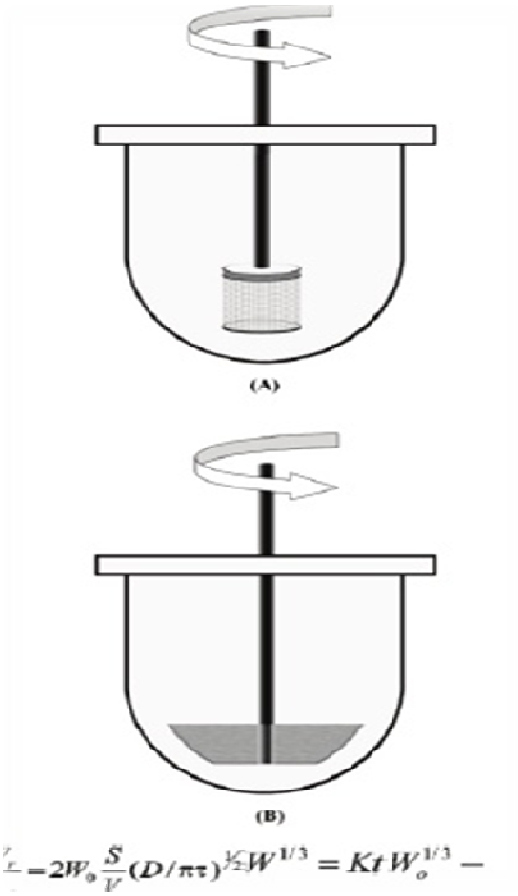

Figure 1. Schematic diagram of (A) USP Apparatus 1 and (B) USP Apparatus 2

• USP Apparatus 2 (Paddle Apparatus)

This apparatus is useful for tablets, capsules, beads and floaters. Solids (mostly floating), monodisperse (tablets) and polydisperse (encapsulated beads) drug products are commonly tested using USP Apparatus 1 (Figure 1). An apparatus described by Levy and Hayes [28] may be considered the forerunner of the beaker method. It consisted of a400 ml beaker and a three-blade, centrally placed polyethylene stirrer (5 cm diameter) rotated at 59 rpm in 250 ml of dissolution fluid (0.1N HCl). The tablet was placed down the side of the beaker and samples were removed periodically. In the Apparatus 2, (the paddle apparatus method) a paddle replaces the basket as the source of agitation. As with the basket apparatus, the shaft should position no more than 2mm at any point from the vertical axis of the vessel and rotate without significant wobble. [8]The apparatus is useful for tablets, capsules and suspensions. Like USP

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- **USP Apparatus 3 (Reciprocating Cylinder Apparatus)**

The design of USP apparatus 3 is based on the disintegration tester. The assembly of USP apparatus 3 consists of a set of cylindrical, flat-bottomed glass outer vessels; a set of glass reciprocating inner cylinders; and stainless steel fittings and screens that are made of suitable material and that are designed to fit the tops and bottoms of the reciprocating cylinders. Operation involves programming the agitation rate, in rpm, of the up and down for the inner tube inside the outer tube. On the up stroke, the bottom mesh in the inner tube moves upward to contact the product and on the down stroke the product leaves the mesh and floats freely within the inner tube. Thus the action produced carries the product being tested through a moving medium.

The USP Apparatus 3, a Reciprocating Cylinder, dips a transparent cylinder containing the dosage form at a rate determined by operator. The tubes a have mesh base to allow the medium to drain into a sampling reservoir as the tube moves up and down, thus creating convective forces for dissolution. The cylinders can also be transfer to different media at specified time automatically. A second design is the rotating bottle apparatus, which also allow for changing of medium to simulate a pH gradient or fed and fasted conditions. [5] It allows automated testing for up to six days and the manufacturers advocate its use in the testing of extended-release dosage forms. It became official in USP 22 as Apparatus 3and is prescribed for the testing of extended-release articles. [10] This apparatus is originally used for extended release products, bead type modified release dosage form, [6] particularly beads in capsules. It is also useful for solids which are mostly non-disintegrating (Figure 2).USP Apparatus 3 offers advantages like i) programmed for dissolution in various media for various time, ii) the media can be changed easily, iii) may start at pH 1 and then pH 4.5 and then at pH6.8 and iv) attempts to mirror pH changes and transit times in the GI tract. But it has got some disadvantages too, i.e. i) disintegrating dosage forms show too low results, ii) surfactants cause foaming and iii) volume of dissolution media is too small.

- **USP Apparatus 4 (Flow-Through Cell Apparatus)**

The history of the flow through cell methodology in drug release testing of oral dosage forms begins in the 1950's. The first attempt for the development of the flow-cell method was probably made in the laboratories of the U.S. Food and Drug Administration in 1957. Since then; various flow-cell devices have been described. The flow through cell was recommended as an alternative in vitro drug release testing apparatus by the Dissolution Tests working group of the Federation International Pharmaceutique (F.I.P.) in 1981. [11] Afterwards, the method was incorporated in various pharmacopoeias. [12] USP Apparatus 4 can be operated underdifferent conditions such as open or closed system mode, different flow rates and temperatures. The diversity of available cell types allows the application of this apparatus for testing of a wide range of dosage forms including tablets, powders, suppositories or hard and soft gelatin capsules. It is the method of choice for extended release and poorly soluble products. [13, 14] USP Apparatus 4 requires the sampling pump to be on continuously throughout the analysis, as the dissolution rate is directly proportional to the flow rate of the medium that is pumped into the flow through cell. Sampling for this technique therefore requires that continuous collection or measurement of the eluted sample be maintained. As the dissolution time increases, large sample storage may be

required, which may not be practical. Fraction collectors have a finite number of positions that are reduced as the volume of samples to be collected increases, which can limit the number of time points that can be collected. Sample splitters can also be used to divert the sample sequentially between collection and waste, thus reducing the volume of sample to be collected. More recently a dual sampling rack has been designed to allow samples to be collected while simultaneously diluting, if required, and injecting into either an HPLC system or a UV spectrophotometer. [15]

Drug products like solids (tablets, capsules, implants, powder, and granules), semisolids (suppositories, soft gelatin capsules, ointments) and liquids (suspensions) are usually tested using this apparatus (Figure 3).

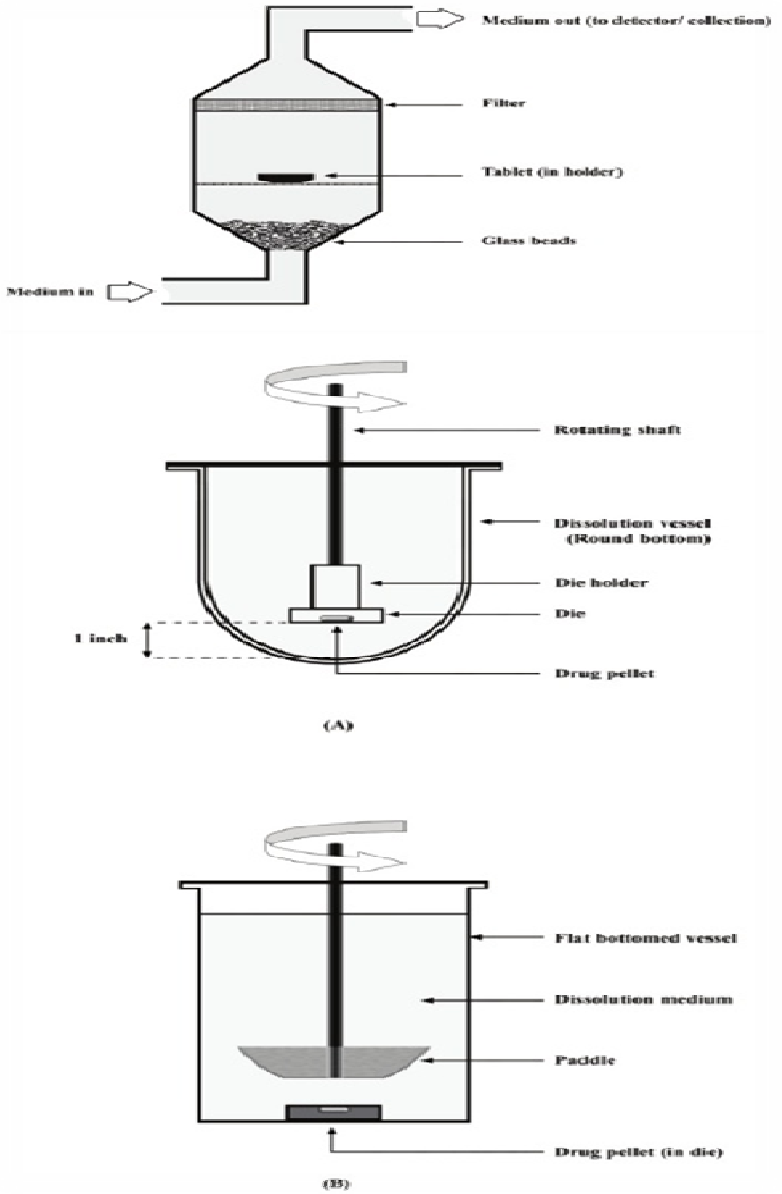

Figure 3. Schematic diagram of USP Apparatus 4 (Flow-Through Cell Apparatus), Schematic diagram of (A) the rotating disk apparatus (Wood Apparatus) and (B) the Stationary disk apparatus

Advantages of the apparatus include: i) no limitation regarding the volume of media used for the dissolution test, ii) suitable for low soluble drugs, iii) gentle hydrodynamic

conditions, iii) simulation of the gastrointestinal transit and iv) suitable for special dosage forms such as powder and granules, implants. But the apparatus has got limited experience; pump precision may influence the results and fractioned primary data lead to greater experimental error when computed to cumulative profiles.

- **USP Apparatus 5 (Paddle-over-Disk Apparatus)**

In Paddle-over-Disk method the paddle and vessel assembly from Apparatus 2 with the addition of a stainless steel disk assembly designed for holding the transdermal system at the bottom of the vessel. The temperature is maintained at 32°C ± 0.5°C. The disk assembly holds the system flat and is positioned such that the release surface is parallel with the bottom of the paddle blade. [16]. The apparatus is used to test transdermal patches. [17]

- **USP Apparatus 6 (Cylinder Apparatus)**

This is a modification of the basket apparatus (USP Apparatus 1).It uses the vessel assembly from Apparatus 1 except to replace the basket and shaft with a stainless steel cylinder stirring element. [16] The apparatus is used to test transdermal patches. [17]

- **USP Apparatus 7 (Reciprocating Holder Apparatus)**

Originally introduced in the USP as small-volume option forsmall transdermal patches, the reciprocating disk apparatus waslater renamed the reciprocating holder apparatus with the adoption of four additional holders for transdermal systems, osmotic pumps, and other low-dose delivery systems. [17] The apparatus is used to test transdermal patches. [18]

CONCLUSION

Dissolution research started to develop in 1897 when Noyes and Whitney derived their equation in the course of their dissolution studies on benzoic acid and lead chloride. Thus, dissolution started as a topic in physical chemistry, and is still an important subject of research in various sections of physical sciences. The goal of dissolution testing is to assure the pharmaceutical quality of the product which includes not only ability to manufacture the product reproducibly and the drug to maintain its release properly throughout its self life but also that the product's biopharmaceutical characteristics, such as rate and extent of absorption, can be relied on. It would, therefore, be desirable to develop dissolution tests that can assess the ability of the dosage form to release the drug completely and to simultaneously indicate how the product will perform in vivo. Dissolution testing is a routine work for pharmaceutical quality control for oral solid dosage forms like tablets, capsules. It is also essential for the transdermal drug delivery systems. The science of dissolution testing is developing every day. Advancement in technology makes the procedure easy, fast and reliable through scientific experiments worldwide. It is an essential tool for pharmaceutical analysis and drug development.

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