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# REVIEW ON DISSOULTION APPARATUS FOR TESTING OF PHARMACEUTICAL DOSAGE FORMS

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**ABSTRACT**

Dissolution testing is an official test used by Pharmacopeia's for evaluating drug release of semisolid and solid dosage forms. The most important applications of the dissolution testing include as a tool to ensure consistent product quality, biopharmaceutical characterization of the drug product and to predict in vivo drug bioavailability. Although initially developed for oral dosage forms, the role of the dissolution test has now been extended to 'drug release' studies on various other forms such as topical and transdermal systems and suppositories.. The aim of this review is to classify various dissolution apparatus and give their specifications according to various pharmacopoeias.

**Key words**: Pharmacopoeia, Pharmaceutical tablets, Dissolution, Apparatus, Dissolution testing.

## INTRODUCTION

The definition of dissolution is deceptively simple. It is defined as the rate of mass transfer from a solid surface into the dissolution medium under standardized conditions of liquid/solid interface, temperature and solvent composition. It is a dynamic property that changes with time and describes the process by which a homogenous mixture of a solid or a liquid can be obtained in a solvent. Dissolution testing is a requirement for all solid oral dosage forms and is used in all phases of development for product release and stability testing [1].For dosage forms containing an active solid ingredient, the rate of dissolution may be important to absorption. Obviously, in most instances, dissolution of the active solid material is affected by a range of factors such as the media in which drug is dissolving, affinity of solid particles to dissolve in media and the temperature of media. There are numerous other factors, such as pH, excipients, and coatings, which have an effect on the rate of dissolution. Over the earlier period of 50 years, dissolution testing has also been employed as a quality control (QC) procedure, in R&D to detect the influence of critical manufacturing variables and in comparative studies for in vitro-in vivo correlation (IVIVC) [2]. The FDA also give guidance on dissolution testing for immediate release solid oral dosage forms includes the use of the Biopharmaceutics Classification System (BCS) guidelines for biorelevant dissolution tests, which is based upon aqueous solubility and intestinal permeability of the drug substance [3]. According to the Biopharmaceutics Classification System the number of bio availability/bioequivalence studies can be reduced by in vitro dissolution testing which may be a useful tool to forecast the in vivo performance of drug products [4].

The most common dissolution apparatus used throughout the world are the paddle and the basket. These methods are easy and robust and are generally flexible enough to allow dissolution testing for a wide variety of drug products. For this reason, Apparatus 1 and 2 should be used for dissolution method development unless shown to be unsatisfactory. Other dissolution techniques and equipment include USP 3 (reciprocating cylinders), USP 4 (flow-through-cell), USP 5 (paddle-over-disk), USP 6 (cylinder) and USP 7 (reciprocating holders) [5]. More drug release equipment, USP Apparatus 5 and 6, deal with transdermal systems. USP Apparatus 7 was developed for the analysis of transdermal systems as well as a variety of drug release systems such as implants and osmotic pumps. Because of the multiplicity of delivery systems and the evolving nature of understanding in the area of drug release, different experimental modifications may be

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needed to obtain a suitable in vivo correlation with in vitro release data. Alternatives or modifications to established methodology should be considered on the basis of proven superiority for a particular product. If the release of the active drug substance from an individual drug product cannot be accommodated by one of the major compendial apparatus, appropriate modifications have to be developed. However, unnecessary proliferation of alternative dissolution apparatus should not be encouraged due to the reproducibility problems that plagued early dissolution equipment; this will also hinder regulatory acceptance.

Drug dissolution testing plays an important role as a routine quality control test, for characterizing the quality of the product and also plays a major role in drug development. It also acts as a primary aid in the characterization of formulations and also in biopharmaceutical characterisation of the drug product. Dissolution testing is a critical preformulation solubility analysis research tool in the process of drug discovery that requires measuring the stability of the investigational product, achieving uniformity in production lots and determining its in vivo availability. It is also useful in the pharmaceutical and biotechnology industry to formulate drug dosage forms and to develop quality control specifications for its manufacturing process. Dissolution testing as an "analytical" measure of product consistency, product quality and manufacturing process control. Predictive of in vivo performance of drug products to reduce unnecessary human studies, accelerate drug development, and hasten evaluation of post-approval changes to detect relevant product changes so as to ensure the quality and consistent performance of products. The dissolution test occupies the topmost position as a sensitive reliable test among the various tests that are performed on the drug solids and also as a predictive tool for in vivo drug bioavailability behaviour [6-10].

The main purpose of this article is to review dissolution apparatus and to present an updated review of non pharmacopeial dissolution methods for testing conventional and novel dosage forms.

**Dissolution apparatus:**

Various official dissolution test apparatus according to IP (Indian Pharmacopoeia), USP (United State pharmacopoeia), BP (British Pharmacopoeia), EP (European Pharmacopoeia) and JP (Japanese Pharmacopoeia) are given in table 1.

USP apparatus (non-official)

- Rotating bottle method
- Diffusion cell
- Peristalsis cell
- Intrinsic dissolution method

**Dissolution Apparatus according to USP:**

**Apparatus 1 (Basket Apparatus):** It consists of a vessel, which is made up of glass or other inert transparent material, a motor, a metallic drive shaft and a cylindrical basket. The vessel is partially immersed in a suitable water bath or heated by a suitable device such as a heating jacket. The water bath or heating device maintain the temperature inside the vessel at 37±0.5°C during the test and keep the bath fluid in a constant and smooth motion. The cylindrical vessel having hemispherical base with the following dimensions and capacities: for anominal capacity of 1 L, the height is 160 mm to 210 mm and its inside diameter is 98 mm to106mm; for a nominal capacity of 2 L, the height is 280 mm to 300 mm and its inside diameter is 98 mm to 106 mm; and for a nominal capacity of 4 L, the height is 280 mm to 300 mm and it's inside diameter is 145 mm to 155mm. Its sides are flanged at the top and a fitted cover may be used to retard evaporation. The shaft is positioned so that its axis is not more than 2 mm at any point from the vertical axis of the vessel and rotates smoothly and without significant wobble that could affect the results. The total height of the basket is 37±3.0mm. A motor with a speed regulator capable of maintaining the speed of rotation within ±4% of that specified in the individual monograph. The vent hole is 2.0±0.5mm. The clear opening is 20.2±0.1mm. Shaft and basket components of the stirring element are fabricated of stainless steel, type 316, or other inert material. A dosage unit is placed in a dry basket at the beginning of each test. The distance between the inside bottom of the vessel and the bottom of the basket is maintained at 25±2 mm during the test.

**Apparatus 2(Paddle type):** The assembly is same as Apparatus 1, except that in the stirring element the basket is replaced by a paddle. The shaft is situated so that its axis is not more than 2 mm from the vertical axis of the vessel and turns easily without huge wobble that could influence the results. The vertical centre line of the blade passes through the axis of the shaft so that the bottom of the blade is flush with the bottom of the shaft. The distance of 25 ± 2 mm between the bottom of the blade and the inside bottom of the vessel is maintained during the test. The height and thickness of the blade is 19.0±0.5 and 4.0±1mm. The radius disk of the paddle is 41.5±0.5mm. The dosage unit is allowed to sink to the bottom of the vessel before rotation of the blade is started. A small, loose piece of nonreactive material having few turns of wire helix may be attached to dosage units that would otherwise float.

**Apparatus 3 (Reciprocating Cylinder):** The assembly consists of a set of cylindrical, flat-bottomed glass vessels; a set of glass reciprocating cylinders; Inert fittings (stainless steel type 316 or other suitable material), and screens that are made of suitable nonsorbing and nonreactive material and that are designed to fit the tops and bottoms of the reciprocating cylinders; and a motor and drive assembly to reciprocate the cylinders vertically inside the vessels. The vessels are partially immersed in a suitable water bath of any convenient size that permits holding the temperature at 37±0.5°C during the test. A device is used that allows the reciprocation rate to be selected and maintained at the specified diprate given in the individual within ±5%.The vessels are provided with an evaporation cap that remains in place for the duration of the test.

**Apparatus 4 (Flow Through Cell):** The assembly consists of a reservoir and a pump for the dissolution medium, a flow through cell, and a water bath that maintains the dissolution medium at 37±0.5°C. The specified cell size is used as given in the individual monograph. The pump forces the dissolution medium upwards through the flow through cell. The delivery range of the pump is between 240 and 960 ml/hour with standard flow rates of 4, 8, and 16 ml/minute. The flow profile is sinusoidal with a pulsation of 120 ± 10 pulses per minute. The flow through cell made up of inert material is mounted vertically with a filter system that is specified in the individual monograph which prevents the escape of un-dissolved particles from the top of the cell. The standard cell diameters are 12 and 22.6 mm and the bottom cone is usually filled with small glass beads of about 1 mm diameter with one bead of about 5 mm positioned at the apex to protect the fluid entry tube. A tablet holder is used to position special dosage forms. The cell is immersed in a water bath to maintain the temperature at 37±0.5℃. The apparatus uses a clamp mechanism and two O-rings to assemble the cell. The pump is separated from the dissolution unit in order to shield the latter against any vibrations originating from the pump. The level of the pump should be lower than the reservoir flasks. Tube connections are as short as possible. Use suitably inert tubing, such as polytef, having 1.6-mminner diameter and chemically inert flanged end connections.

**Apparatus 5 (Paddle Over Disk Method):** The paddle and vessel assembly from paddle apparatus with the addition of a stainless steel disk assembly designed for holding the transdermal system at the bottom of the vessel. The temperature should be maintained at 32±0.5°C. During the test maintain a distance of 25±2mm between the paddle blade and the surface of the disk assembly. The vessel may be covered during the test to minimize evaporation. The disk assembly for holding the transdermal system is designed to minimize any dead volume between the disk assembly and the bottom of the vessel. The disk assembly holds the system flat and is positioned so that the release surface is parallel with the bottom of the paddle blade.

**Apparatus 6 (Rotating Cylinder Method):**The vessel assembly used is same as basket apparatus except the basket and shaft is replaced with a stainless steel cylinder on which dosage form is kept. The temperature is maintained at 32 ± 0.5 °C during the test. The dosage unit is placed on the cylinder at the beginning of each test. The distance between the inside bottom of the vessel and the cylinder is maintained at 25±2mm during the test.

**Apparatus 7 (Reciprocating Holder Method):** The assembly consists of a set of volumetrically calibrated containers which are made of glass or other suitable inert material, a motor and drive assembly to reciprocate the system vertically and to index the system horizontally to a different row of vessels automatically if desired, and a set of suitable sample holders. The solution containers are partially immersed in a water bath of suitable size to maintain the temperature at 32±0.5°C. No part of the assembly, including the environment in which the assembly is placed, should contribute motion, agitation, or vibration beyond that due to the vertically reciprocating sample holder. An apparatus that permits observation of the system and holder during the test is preferable. The size container and sample holder are used as specified in the individual monograph.

**Dissolution Apparatus according to I.P.**

**1) Apparatus 1(Paddle type):** The design and measurements of this apparatus is same as USP apparatus 2(Paddle type) except the height of the vessel and blade is 168±8mm and 19.0mm and the radius disk of the paddle is 41.5mm.

**2) Apparatus 2(Basket type):** The design and measurements of this apparatus is same as USP apparatus 1(Basket type) except the height of the basket is36.8±3.0mm, the clear opening is 22.2±1.0mm and the vent hole which is attached to shaft is 2.0mm.

**Rotating bottle method:** This method is mainly used for controlled liberate beads. This process is suggested in NF-Xlll. The equipment consists of a rotating rack that holds the sample drug products in bottle. The bottles are capped tightly and rotated in a 37°C heat bath. Samples are decanted through a 40 mesh screen and the residues are assayed. The medium is replaced with equivalent amount of withdrawn sample. A dissolution test with pH 1.2 medium for 1 hr., pH 7.0 medium for 1.5 hours, pH 7.5 medium for 2 hours be suggested to simulate condition of the GIT.

**Vertical Diffusion cell:** The assembly consists of two chambers (a donor chamber and a receptor chamber) which is separated by a donor compartment and held together by a clamp. It is commonly used for testing the *invitro* release rate of topical drug products such as creams, gels, and ointments. Alternative diffusion cells of the same general design and size can be used. It is made from borosilicate glass, although different materials may be used to manufacture the body and other parts of the cell assembly. The apparatus should not react with the test product or samples. In the donor compartment, the semisolid dosage form sample placed on a synthetic membrane within the cavity of the dosage compartment that is covered with a glass disk. The diameters of the orifices of the donor chamber and the dosage compartment which defines the dosage delivery area for the test should be sized within ±5% of the specified diameter. The receptor chamber orifice should never be smaller than the orifice of the donor chamber and should be fabricated to the same size as the donor chamber orifice. The design of the assembly should facilitate proper alignment of the dosage compartment and receptor orifices. The thickness of the dosage compartment is 1.5 mm which may vary within ± 10% of the specified thickness. The cell body should be manufactured consistently with uniform height

and geometry. Cells should appear the same and their internal receptor volumes should fall within +5% of their specified volume.

**Peristalsis cell:** This method stimulates the hydrodynamic conditions of GIT in an *in vitro* dissolution device. The apparatus consists of rigid plastic cylindrical tubing fitted with a septum and rubber stoppers at both ends. The dissolution chamber consists of a space between the septum & the lower stopper. The equipment is placed in a beaker containing the dissolution medium. The dissolution medium is pumped by way of peristaltic action through the dosage form.

**Intrinsic dissolution method:** It consists of a punch and die fabricated out of hardened steel. The base of the die has three threaded holes for the attachment of a surface plate made of polished steel to provide a mirror smooth base for the compacted pellet. The die has a 0.1cm to 1.0cm diameter cavity into which a measured amount of sample is placed to determine the intrinsic dissolution rate. The punch is then inserted in the die cavity and the sample is compressed with a bench top tablet press. A compacted pellet of the sample is formed in the cavity with a single face of defined area exposed on the bottom of the die. The bottom of the die cavity is threaded so that at least 50% to 75% of the compacted pellet can dissolve without its falling out of the die. The top of the die has a threaded shoulder that allows it to be attached to a holder. The holder is mounted on a laboratory stirring device and the entire die with the compacted pellet is immersed in the dissolution medium and rotated by the stirring device.

**Table 1. List of official dissolution apparatus[11,12,13,14]**

| Various Official Dissolution Test apparatus | | | | | |
|---|---|---|---|---|---|
| | IP | USP | BP | EP | JP |
| Type 1 | Paddle Apparatus | Basket Apparatus | Basket Apparatus | Basket Apparatus | Basket Apparatus |
| Type 2 | Basket Apparatus | Paddle Apparatus | Paddle Apparatus | Paddle Apparatus | Paddle Apparatus |
| Type 3 | | Reciprocating cylinder | Flow through cell Apparatus | Flow through cell Apparatus | Flow through cell Apparatus |
| Type 4 | | Flow through cell Apparatus | | | |
| Type 5 | | Paddle over disk | | | |
| Type 6 | | Rotating cylinder | | | |
| Type 7 | | Reciprocating Holder | | | |

**Table 2. Details of construction of Paddle type apparatus:**

| Characteristic | USP | BP | IP | EP | JP |
|---|---|---|---|---|---|
| Vessel height | 160-210mm | 160-210mm | 160- 176mm | 160-210mm | 160-210mm |
| Paddle shaft diameter (before coating) | 9.4-10.1mm | 9.4-10.1mm | 9.4-10.1mm | 9.4-10.1mm | 9.4-10.1mm |
| Blade upper chord | 74.5-75.0 mm | 74.5-75.0 mm | 74.5-75.0 mm | 74.5-75.0 mm | 74.5-75.0 mm |
| Blade lower chord | 42 ± 0.1 mm | 42.0 mm | 42.0 mm | 42 ± 0.1mm | 42 ± 0.1mm |
| Height | 19.0 ± 0.5mm | 19.0 ± 0.5 mm | 19.0 mm | 19.0 ± 0.5mm | 19.0 ± 0.5mm |
| Radius disk | 41.5 ± 1mm | 41.5mm | 41.5mm | 41.5 ± 1mm | 41.5 ± 1mm |
| Thickness of blade | 4.0 ± 1mm | 4.0 ± 1mm | 4.1 ± 1mm | 4.0 ± 1mm | 4.0 ± 1mm |
| Device distance from bottom | 25± 2mm | 25± 2mm | 25 ± 2mm | 25± 2mm | 25± 2mm |

**Table 3. Details of construction of Basket type Apparatus**

| Characteristic | USP | BP | IP | EP | JP |
|---|---|---|---|---|---|
| Basket shaft | 6.3-6.5 or 9.4-10.1 mm | 6.3-6.5 or 9.4-10.1 mm | 9.7 ± 0.3 or 6.4 ± 0.1 mm | 6.3-6.5 or 9.4-10.1 mm | 6.3-6.5 or 9.4-10.1 mm |
| Basket material (stainless steel) | Type 316 | Type 316 | Type 316 | Type 316 | Type 316 |
| Vent hole | 2.0 ± 0.5 mm | 2.0± 0.5 mm | 2.0 mm | 2.0 ± 0.5 mm | 2.0 ± 0.5 mm |
| Retention Spring | 3 tangs | 3 tangs | 3 tangs | 3 tangs | 3 tangs |
| Clear opening | 20.2 ± 0.1 mm | 20.2 ± 1.0 mm | 22.2 ± 1.0 mm | 20.2 ± 0.1 mm | 20.2 ± 0.1 mm |
| Wire diameter | 0.25 mm | 0.25 mm | 0.254mm | 0.25 mm | 0.25 mm |
| RPM | 100 | 100 | 100 | 100 | 100 |
| Height of screen | 27.0 ± 1.0mm | 27.0 ± 1.0mm | 27.0 ± 1.0mm | 27.0 ± 1.0mm | 27.0 ± 1.0mm |
| Height of upper cap | 5.1 ± 0.5mm | 5.1 ± 0.5mm | 5.1 ± 0.5mm | 5.1 ± 0.5mm | 5.1 ± 0.5mm |
| Total height of basket | 37.0 ± 3.0mm | 37.0 ± 3.0mm | 36.8± 0.33.0mm | 37.0 ± 3.0mm | 37.0 ± 3.0mm |

**Table 4. Details of construction of Flow through cell apparatus**

| Characteristic | USP | BP | EP | JP |
|---|---|---|---|---|
| Sieve 40 mesh diameter | 0.2 | 0.2 | 0.2 | 0.2 |
| Internal diameter | 20 ± 0.2 | 20 ± 0.2 | 20 ± 0.2 | 20 ± 0.2 |
| Outer diameter | 22.5 ± 0.2 | 22.5 ± 0.2 | 22.5 ± 0.2 | 22.5 ± 0.2 |
| Angle | 40 ± 1$^o$ | 40 ± 1$^o$ | 40 ± 1$^o$ | 40 ± 1$^o$ |
| Tablet holder height | 6.5 mm | 6.5 mm | 6.5 mm | 6.5 mm |
| Tablet holder thickness | 0.5 mm | 0.5 mm | 0.5 mm | 0.5 mm |
| Tablet holder width | 7.5 mm | 7.5 mm | 7.5 mm | 7.5 mm |

**Table 5. Comparison of common specification of various dissolution apparatus**

| Characteristic | USP | IP | BP | EP | JP |
|---|---|---|---|---|---|
| Dissolution vessel | Nominal capacity 1 L – 4 L | Nominal capacity 1 L | Nominal capacity 1 L | Nominal capacity 1 L | Nominal capacity 1 L |
| Shaft position | NMT 2mm from vertical axis | NMT 2mm from vertical axis | NMT 2mm from vertical axis | NMT 2mm from vertical axis | NMT 2mm from vertical axis |
| Allowable variation in (RPM) | ±4%. | ±4%. | ±4%. | ±4%. | ±4%. |
| Shaft rotation speed | 50-100 | 50-100 | 50-150 | 50-100 | --- |
| Distance of bottom of apparatus to inside bottom of apparatus. | 25 ± 2 mm | 25 ± 2 mm | 25 ± 2 mm | 25 ± 2 mm | 25 ± 2 mm |
| Apparatus suitability test | Specified | Not specified | Not Specified | Not Specified | Not Specified |
| Temperature maintained | 37 ± 0.5 | 37 ± 0.5 | 37 ± 0.5 | 37 ± 0.5 | 37 ± 0.5 |

**Figure 1. Schematic view of Rotating Basket Designed**

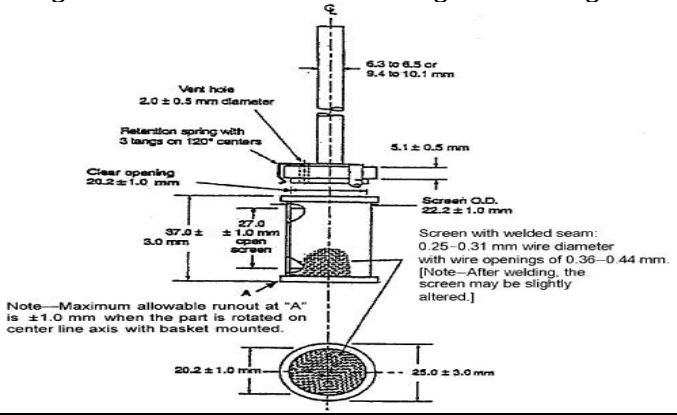



**Figure 2. Schematic view of Rotating Paddle Designed**

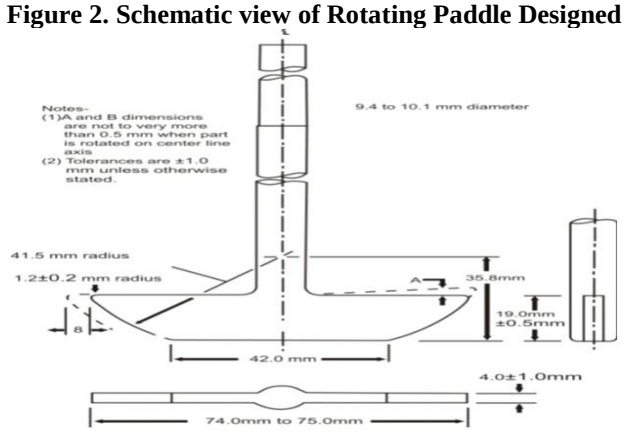



**Figure 3. Schematic view of Reciprocating Cylinder Designed**

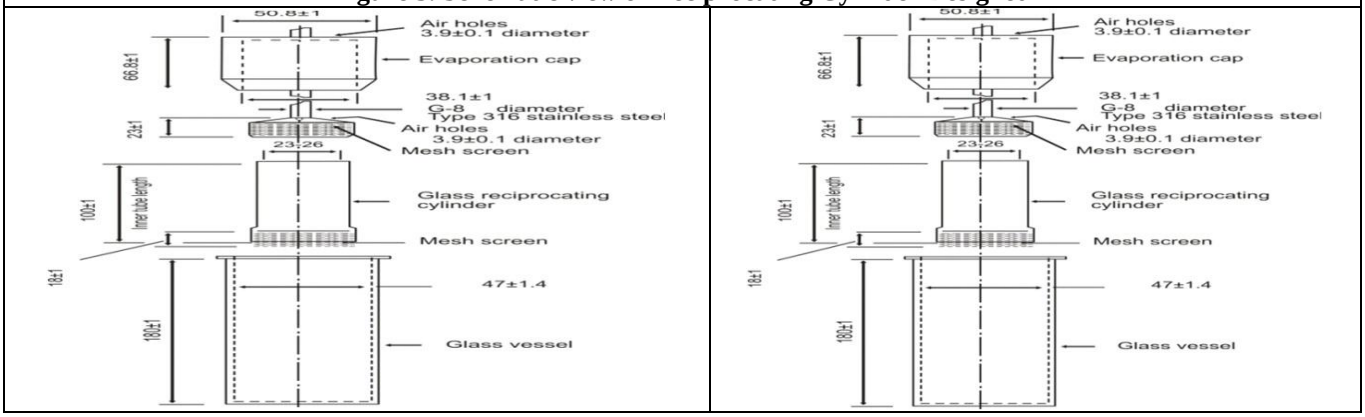


**Figure 4. Schematic view of Flow-Through Cell Designed**

Small cell for tablets and capsules (top) Tablet holder for the small cell (bottom) (All measurements are expressed in mm unless noted otherwise.)

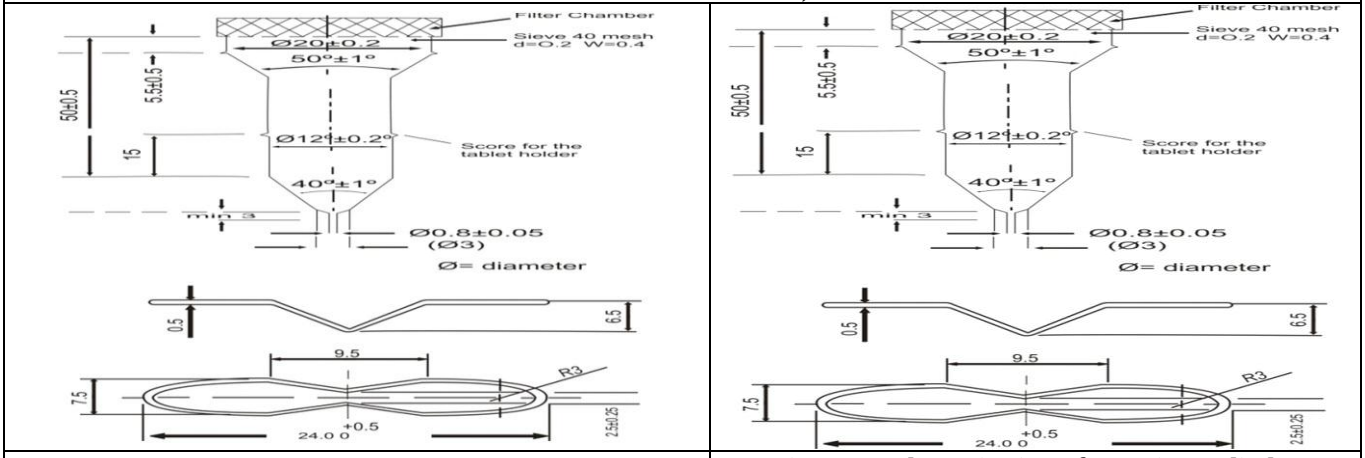



**Figure 5. Schematic view of Paddle over Disk Designed**

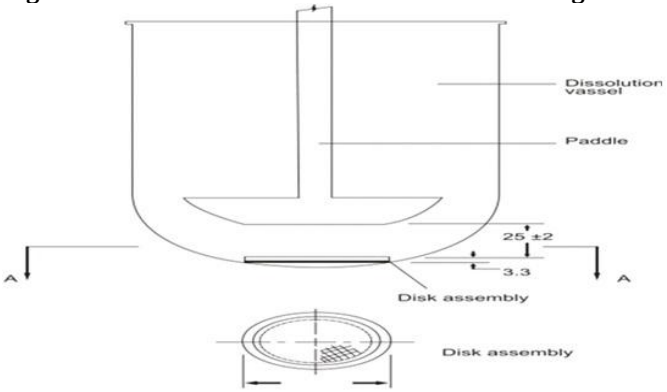



**Figure 6. Schematic view of Rotating Cylinder Designed**

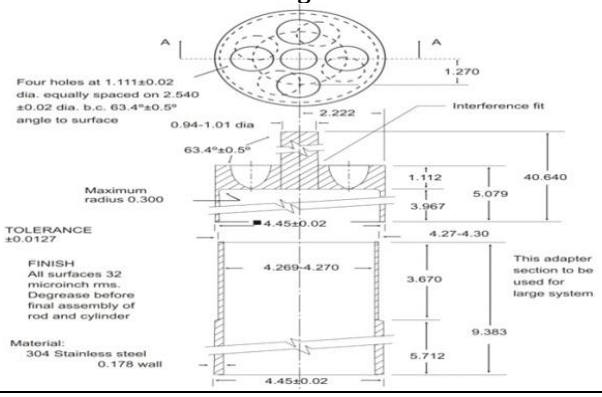



**Figure 7. Schematic view of Reciprocating Holder Method**

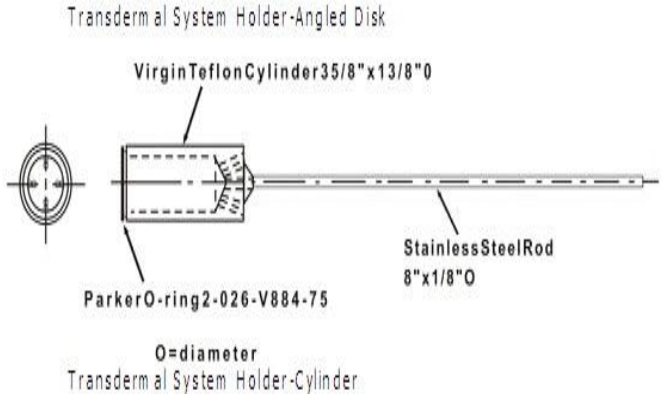



**Figure 8. Schematic view of Vertical Diffusion cell**

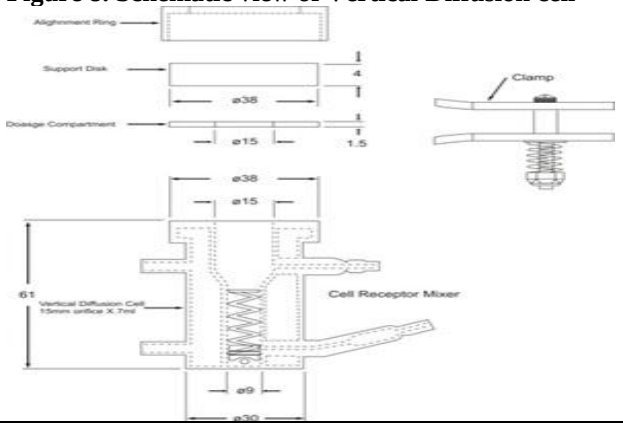
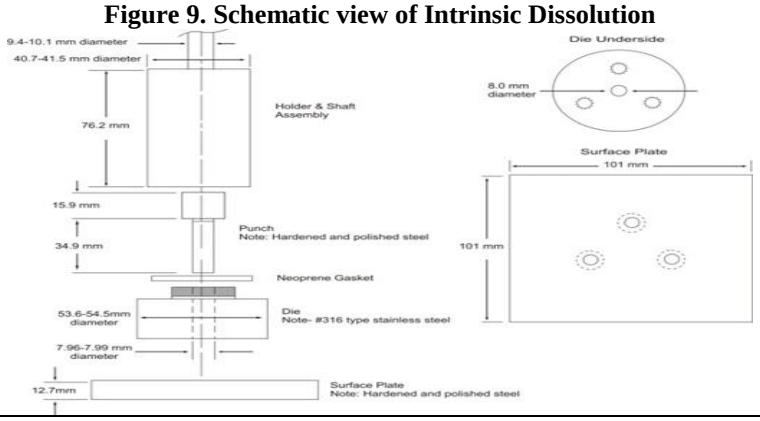



**Figure 9. Schematic view of Intrinsic Dissolution**



## CONCLUSION

Planning an appropriate dissolution method takes into depiction numerous API, formulation, and analytical methodology parameters. In vitro dissolution testing plays assumes a vital role in assuring product quality and performance. Attempt should be made to investigate bio-relevant dissolution testing that mechanistically resembles in vivo conditions. Properly designed dissolution tests will accelerate drug development, hasten validation of post-approval changes and possibly reduce unnecessary human studies.

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**CONFLICT OF INTEREST**:
The authors declare that they have no conflict of interest.

## REFERENCES

1. U.S. FDA/CDER, Guidance for Industry, Dissolution testing of immediate release solid oral dosage forms, 1997.
2. Zhang H, Yu L. Dissolution Testing for Solid Oral Drug Products: Theoretical Considerations. *American Pharmaceutical Review*, 7(5), 2004, 26-31.
3. Wang Q, Fotaki N, Mao Y. Biorelevant Dissolution: Methodology and Application in Drug Development, Dissolution Technologies, 2009, 6-12.
4. U.S. FDA/CDER. Guidance for Industry: Immediate release solid oral dosage forms, Scale-up and post approval changes: chemistry, manufacturing, and controls, in vitro dissolution testing and in vivo bioequivalence documentation.1995.
5. Kumar D, Singh J, Antil M, Kumar V. Quality control of tablets. *International Journal of Universal Pharmacy and Bio Sciences*, 5(4), 2016, 53-67.
6. Siewert M, Dressman J, Brown C, Shah VP. FIP/AAPS guidelines for dissolution/in vitro release testing of novel/special dosage forms. *Dissolution Technologies*, 10(1), 2003, 6–15, 2.
7. Williams R.L, Foster T.S. Dissolution; a continuing perspective. *Dissolution technology*, 10, 2004, 6-14.
8. FIP guidelines for dissolution testing of solid oral products. *Pharm. Ind*, 42, 1981, 334- 343.
9. Azarmi, Wilson Roac, Raimar L obenberg. Current perspectives in dissolution testing of conventional and novel dosage forms. *International Journal of Pharmaceutics*, 2006, 5.
10. FIP/AAPS Guidelines for Dissolution/In Vitro Release Testing of Novel/Special Dosage Forms, Dissolution Technologies. February 2000.
11. Indian Pharmacopoeia - 2007, Volume-1,179 -182.
12. United States Pharmacopoeia (USP XXVI), 2155 -2165.
13. European Pharmacopoeia - 5.0, 228 to 233.
14. British Pharmacopoeia - 1993, VOL-II, A160.