

QUALITY CONTROL TESTS FOR TABLETS



QUALITY CONTROL OF TABLETS

- Thickness and diameter
- Weight variation
- Hardness
- Friability
- Drug content
- Disintegration time
- In- vitro dissolution

General Appearance:

-Size, shape, and thickness:

This is important to facilitate packaging and to decide which tablet compressing machine to use.

-Organoleptic properties:

which include color, taste and odor of the tablets.

⊙ Thickness can vary with no change in weight

due to:

a- Difference in the density of the granulation

b- The pressure applied to the tablets.

c- The speed of tablet compression.

- ◉ tablet thickness important in reproducing tablets **identical in appearance** but also to insure that every production lot will be usable with selected packaging components.
- ◉ If the tablets are thicker than specified, a given number no longer may be contained in the volume of a given size bottle.
- ◉ **A plus or minus 5% may be allowed, depending on the size of the tablet.**



Hardness (crushing strength):

It is the load required to crush the tablet when placed on its edge.

Why do we measure hardness?

- To determine the need for pressure adjustments on the tableting machine.
- To withstand the mechanical shocks of manufacturing, packaging, and shipping,
- To ensure consumer acceptance.

- Hardness can affect the disintegration. So if the tablet is too hard, it may not disintegrate in the required period of time. And if the tablet is too soft, it will not withstand the handling during subsequent processing such as coating or packaging.

>In general, if the tablet hardness is too high, we first check its disintegration before rejecting the patch. And if the disintegration is within limit, we accept the patch.



Factors Affecting the Hardness:

- ⊙ Compression of the tablet and compressive force.
- ⊙ Amount of binder. (More binder à more hardness)
- ⊙ Method of granulation in preparing the tablet (wet method gives more hardness than direct method, Slugging method gives the best hardness).
- ⊙ Limits:

Oral tablets have a hardness of 4 to 10kg ; but, hypodermic and chewable tablets have a hardness of 3 kg and sustained release tablets have about 10-20 kg.

>Make hardness test on 5 tablets and then take the average hardness.

⊙ *Friability:*

It is the tendency of tablets to powder, chip, or fragment and this can affect the elegance appearance, consumer acceptance of the tablet, and also add to tablet's weight variation or content uniformity problems.

- Friability is a property that is related to the hardness of the tablet.
- An instrument called friabilator is used to evaluate the ability of the tablet to withstand abrasion in packaging, handling, and shipping.
- friabilator determine friability by allowing the tablet to roll and fall 6 inches within a rotating tumbling apparatus.



Procedure:

1. Weigh 20 tab altogether
2. Put these tablets in the friabilator and adjust the instrument at 100 rpm (i.e. = 25 rpm for 4 min)

3. Weigh the 20 tablets (only the intact ones)

$$F = 100 \times (1 - w/w_0)$$

Where w_0 = weight of tablets before friability

w = weight of tablets after friability

4. Friability (% loss) = It must be less than or equal to 1% but

Some chewable tablets and most effervescent tablets are highly friable and require special unit packaging.

Weight Variation

(uniformity of weight) of tablets:

The weight variation test would be a satisfactory method for determining drug content uniformity of drug distribution.

Weight variation test is applicable when the tablets containing **50 mg or more** of drug substance or when the drug substance represents **50% or more** (by weight) of the dosage form unit.

1. Weigh 20 tablet selected at random, each one individually .
 $X_1, X_2, X_3 \dots X_z$
2. Determine the average weight. $X = (X_1 + X_2 + X_3 + \dots + X_z) / 20$

Limits according to U.S.P

Average Weight	Percentage Difference
130 mg or less	± 10
More than 130 mg through 324 mg	± 7.5
More than 324 mg	± 5

○ Limit:

○ Upper limit = average weight + (average weight * %error)

○ Lower limit = average weight - (average weight * %error)

○ The individual weights are compared with the upper and lower limits.

>>Not more than two of the tablets differ from the average weight by more than the % error listed, and no tablet differs by more than double that percentage.

Tablets that are coated are exempt from these requirements but must conform to the test for content uniformity if it is applicable.

Content Uniformity Test:

Randomly select 30 tablets. 10 of these assayed individually. The Tablet pass the test if 9 of the 10 tablets must contain not less than 85% and not more than 115% of the labeled drug content and the 10th tablet may not contain less than 75% and more than 125% of the labeled content.

If these conditions are not met, remaining 20 tablet assayed individually and none may fall out side of the 85 to 115% range.

it is required for all coated and uncoated tablets containing less than 50 mg of an active ingredient comprising less than 50% of the weight of one dosage unit.

Nine of 10 must contain **labeled amount $\pm 15\%$ and **none exceed $\pm 25\%$** .**

Disintegration:

It is the time required for the tablet to break into particles, the disintegration test is a measure only of the time required under a given set of conditions for a group of tablets to disintegrate into particles which will **pass** through **10 mesh screen**. .

The Disintegration apparatus consists of a basket rack holding six plastic tubes, open at the top and bottom; the bottom of the tubes is covered with 10-mesh screen

The basket rack is immersed in a bath of suitable liquid, held at 37°, preferably in a 1 -L beaker. The rack moves up and down in the fluid at a specified rate.

For compressed uncoated tablets the testing fluid is usually **water** at 37°, but in some cases the monographs direct that **simulated gastric fluid** be used.

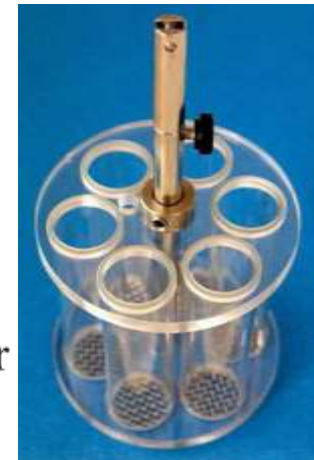


- Liquids used in disintegration

- Water,
- simulated gastric fluid (PH = 1.2 HCl),
- or Simulated intestinal fluid



Six tubes opened at the upper end and closed by a screen at the lower



- For **most uncoated** tablets the period is not more than **30 minutes according to USP** (to **Bp 15 minutes**), although the time for some uncoated tablets varies greatly, from this. For **coated** tablets **up to 2 hours** may be required, while for sublingual tablets, the disintegration time is **3** minutes.
- The tablet disintegration test is limited to manufacturing control of lot-to-lot variations in individual products and is not a measure of bioavailability.
- It is used to provide a simple and useful means for monitoring and controlling the quality of tablets

U.S.P. method for uncoated tablets:

- ⦿ Start the disintegration test on 6 tablets.
- ⦿ If one or two tablets from the 6 tablets fail disintegrate completely within 30min repeat the same test on another 12 tablet. (i.e. the whole test will consume 18 tablets).
- ⦿ Not less than 16 tablets disintegrate completely within the time
- ⦿ if more then two tablets (from the 18) fail to disintegrate, the batch must be rejected.

○ Limits:

For Uncoated tablets:

	Medium	Temperature	Time limit
According to U.S.P.	Simulated gastric fluid	37°C	Not exceed 30min
According to B.P.	water	37°C	Not exceed 15min

6) Dissolution test

- Dissolution is the process by which a solid enters a solution .
- **The dissolution rate** is defined as **the amount of drug substance that goes into solution per time** under standardized conditions of liquid / solid interface, temperature, and solvent composition .
- Dissolution is one of most important **quality control tests** and consider as tool for **predicating bioavailability** , in some cases, replacing clinical studies to determine bioequivalence.
- In fact, a direct relationship between in vitro dissolution rate of many drugs and their bioavailability has been demonstrated and is generally referred as in vitro- in vivo correlation, IVIVC.

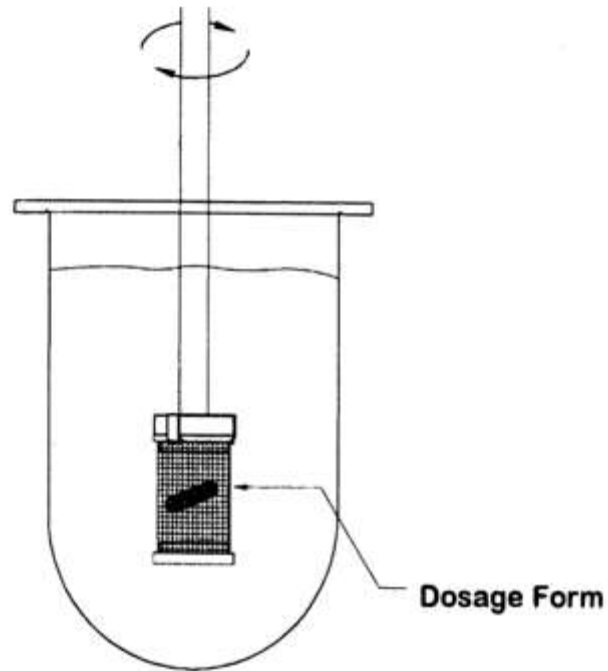
A variety of designs of apparatus for dissolution testing is varying from simple beaker to complex system where an attempt is made to mimic the biological media. The choice of the apparatus to be used depends largely on **the physicochemical properties of the dosage form.**

DISSOLUTION APPARATUS

Apparatus ^a	Name	Drug Product
Apparatus 1	Rotating basket	Tablets
Apparatus 2	Paddle	Tablets, capsules, modified drug products, suspensions
Apparatus 3	Reciprocating cylinder	Extended-release drug products
Apparatus 4	Flow cell	Drug products containing low-water-soluble drugs
Apparatus 5	Paddle over disk	Transdermal drug products
Apparatus 6	Cylinder	Transdermal drug products
Apparatus 7	Reciprocating disk	Transdermal drug products
Rotating bottle	(Non-USP-NF)	Extended-release drug products (beads)
Diffusion cell (Franz)	(Non-USP-NF)	Ointments, creams, transdermal drug products

^aApparatus 1–7 refer to compendial dissolution apparatus in USP-NF (United States Pharmacopeia)

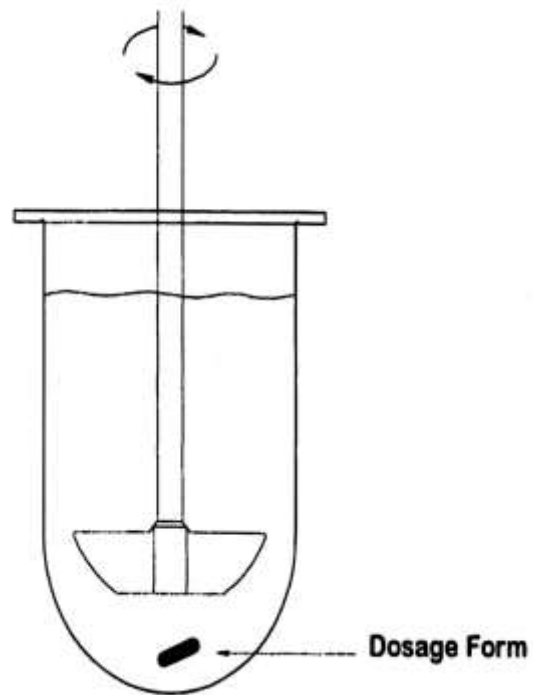
ROTATING BASKET (APPARATUS 1)



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- In case of none-disintegrating dosage forms this apparatus is superior to apparatus 2 since it constraints the dosage form in a steady state fluid flow
- It is inferior for testing dosage forms which contains gums due to clogging of screen matrix

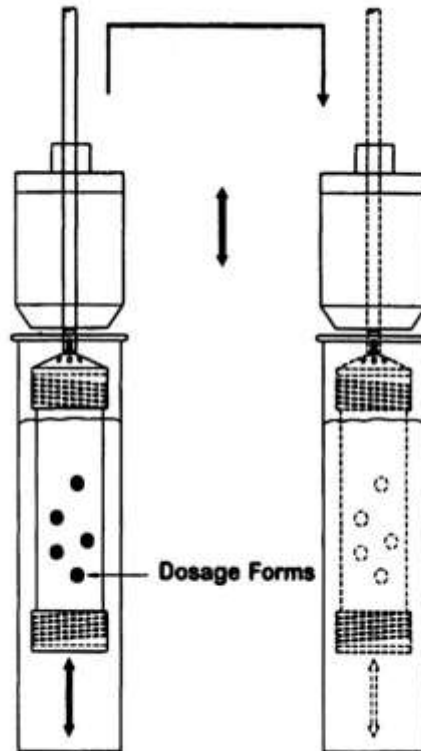
ROTATING PADDLE (APPARATUS 2)



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- ⦿ This apparatus is identical to apparatus 1 except that the paddle is substituted for the rotating basket
- ⦿ Frequently used for both disintegrating and non-disintegrating dosage forms

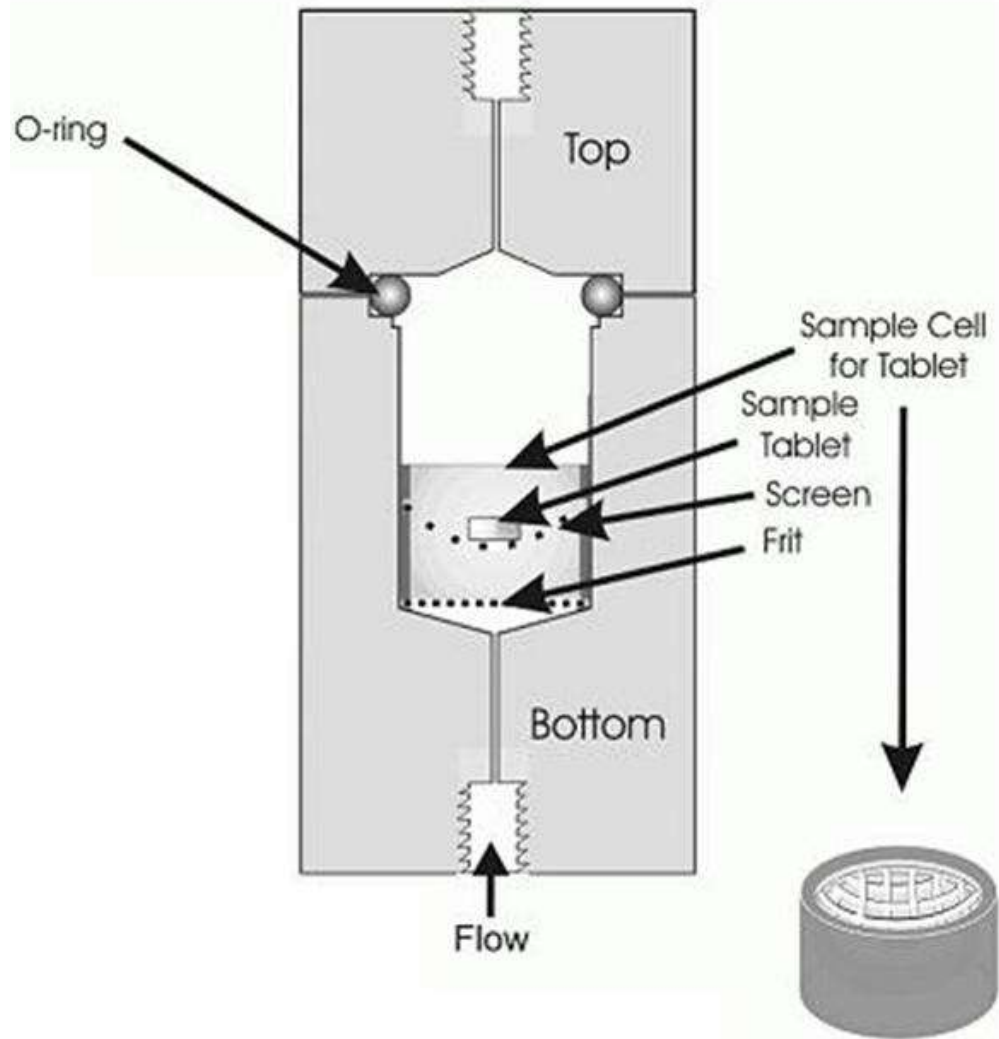
RECIPROCATING CYLINDER (APPARATUS 3)



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- ⦿ One advantage of the reciprocating cylinder is that the gastrointestinal tract conditions can be easily simulated, as it is easy to make time dependent pH changes
- ⦿ This apparatus is most suitable for nondisintegrating (extended release) or delayed release (enteric coated) dosage forms

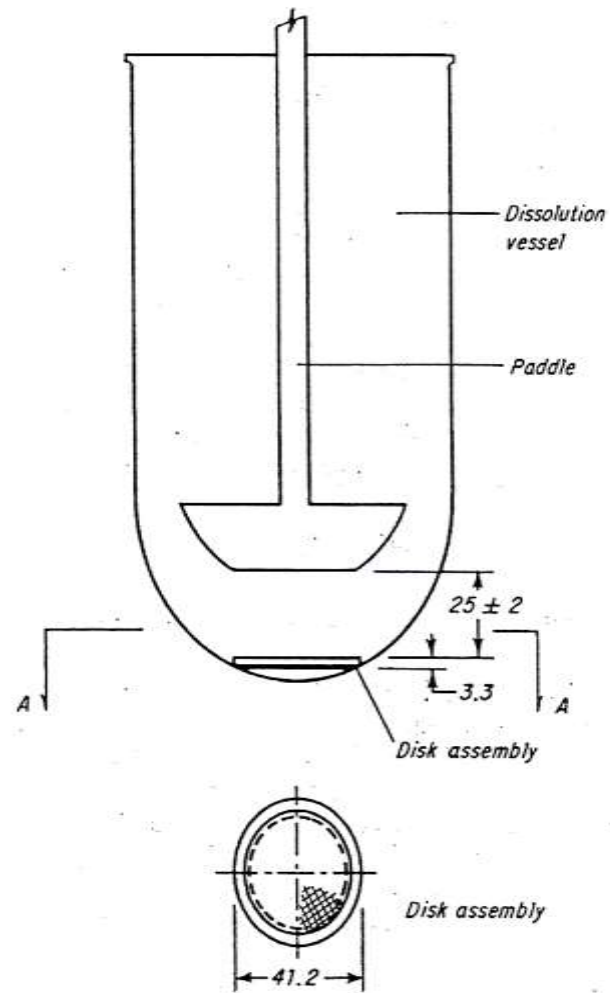
FLOW CELL (APPARATUS 4)



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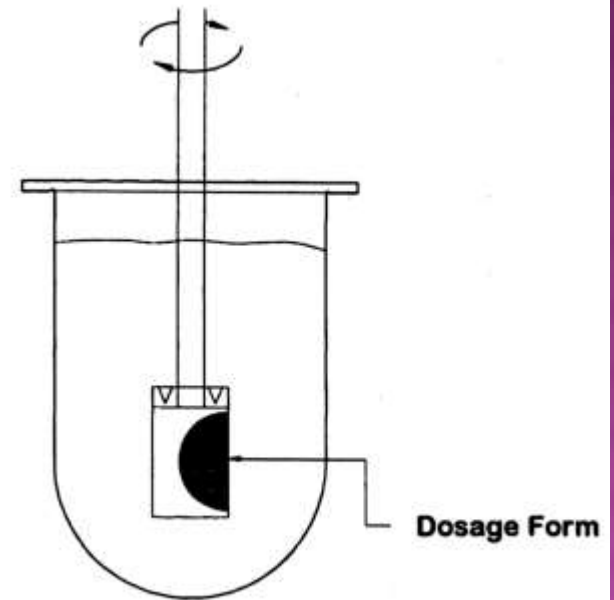
- ⦿ The advantage of flow through cell apparatus is the ability to test drugs of very low aqueous solubility and the ability to change the pH conveniently during the test

PADDLE OVER DISK (APPARATUS 5)



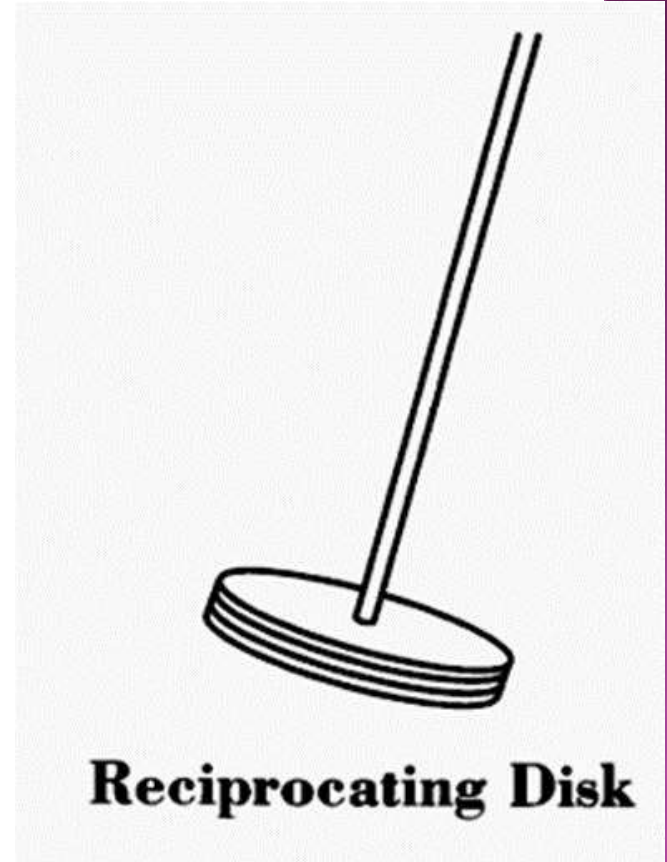
CYLINDER (APPARATUS 6)

- ◉ The cylinder method (Apparatus 6) for testing transdermal preparation is modified from the basket method (Apparatus 1). In place of the basket, a stainless steel cylinder is used to hold the sample.



RECIPROCATING DISK METHOD (APPARATUS 7)

- ◉ In the reciprocating disk method for testing transdermal products, a motor drive assembly (Apparatus 7) is used to reciprocate the system vertically, and the samples are placed on disk-shaped holders using cuprophan supports



- All 6 tablets must meet the requirements specific. If one or two tablets failed, repeat the test on 6 additional tablets . In most cases the amount of drug dissolved should not be less than 70% of quantity contained in tablet after 45min.

The formulation and manufacturing factors affecting the dissolution of a tablet

- a) The particle size of the drug substance
- b) The solubility and hygroscopicity of the formulation
- c) The type and concentration of the disintegrant, binder and lubricant used
- d) The manufacturing method, particularly, the compactness of the granulation and the compression force

- Various pharmacopoeias contain specifications on dissolution requirements of various drugs. (monograph specifies : **stirring speed, temperature, viscosity, pH, composition of dissolution media and presence or absence of wetting agent**)

Thank you

