IN-VITRO DISSOLUTION TESTING MODELS

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Definition-

- Dissolution is a process in which a solid substance solubilizes in a given solvent i.e. mass transfer from the solid surface to the liquid phase.

- Rate of dissolution is the amount of drug substance that goes in solution per unit time under standardized conditions of liquid/solid interface, temperature and solvent composition.

Factors to be considered while designing of a dissolution test

1. Factors relating to the dissolution apparatus
2. Factors relating to the dissolution fluid
3. Process Parameters

1. FACTORS RELATING TO THE DISSOLUTION APPARATUS

- Design of the container
- Size of the container
- Shape of the container
- Nature of agitation
- Speed of agitation
- Performance precision of the apparatus

2. FACTORS RELATING TO THE DISSOLUTION FLUID

- Volume
- Temperature
- Deaeration of dissolution medium
- pH

3. Process Parameters

- Method of introduction of dosage form
- Sampling Techniques
- Changing the dissolution fluid

CLASSIFICATION

There are basically three general categories of dissolution apparatus :

1. Closed-compartment apparatus
2. Open-compartment (continuous flow-through) apparatus
3. Dialysis systems

1. Closed-compartment apparatus

Limited volume apparatus operating under non-sink conditions.

ROTATING BASKET APPARATUS (APPARATUS 1)

First described by Pernarowski

- It is basically a closed-compartment, beaker type apparatus.
- It comprising of a cylindrical glass vessel with hemispherical bottom of one litre capacity partially immersed in a water bath.
- A cylindrical basket made of #22 mesh is located centrally in the vessel at a distance of 2 cm from the bottom and rotated by a variable speed motor through a shaft.

CONTD.....

- All metal parts like basket and shaft are made of stainless steel.

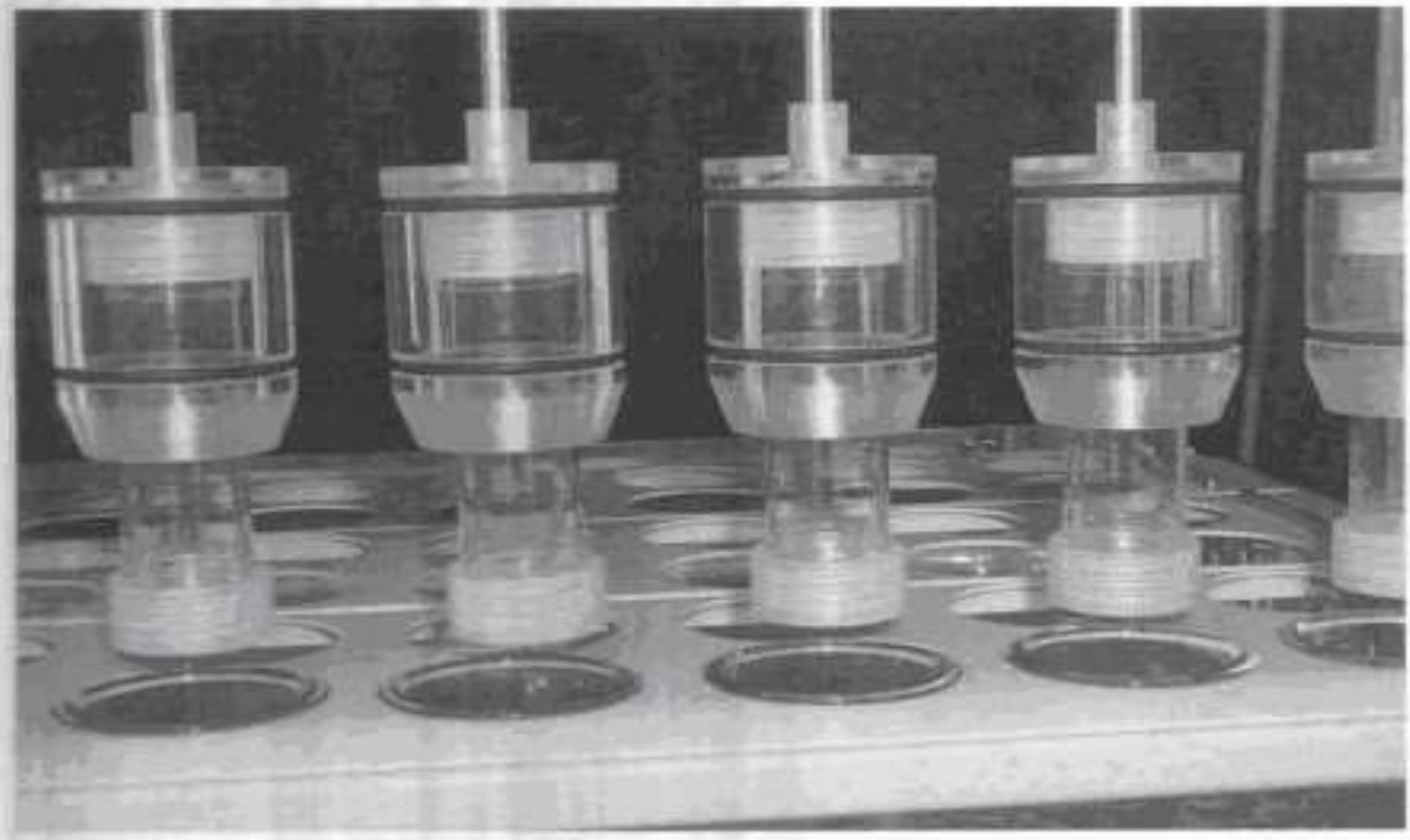
ROTATING PADDLE APPARATUS(APPARATUS 2)

- First described by Levy and Hayes
- Here, basket is replaced with a paddle which acts as a stirrer.
- A small, loose, wire helix may be attached to the dosage form that would otherwise float.
- The position and alignment of the paddle are specified in the official books.

THE RECIPROCATING CYLINDER METHOD (APPARATUS 3)

- This method adopts the USP disintegration "basket and rack" assembly for the dissolution test.
- The disks are not used.
- This method is less suitable for precise dissolution testing due to the amount of agitation and vibration involved.
- Used for dissolution testing of controlled-release bead-type (pellet) formulation.
- E.g. Chlorpheniramine ER tablets, Carbamazepine chewable tablet

(c) The reciprocating cylinder (USP III) dissolution apparatus.



PADDLE OVER DISK METHOD

(APPARATUS 5)

- Modification of Apparatus 2.
- Here, stainless steel disk designed for holding transdermal system at the bottom of the vessel.
- The disk/device should not , react with, or interfere with the specimen being tested.
- The disk holds the system flat and is positioned such that the release surface is parallel with the bottom of the paddle blade.

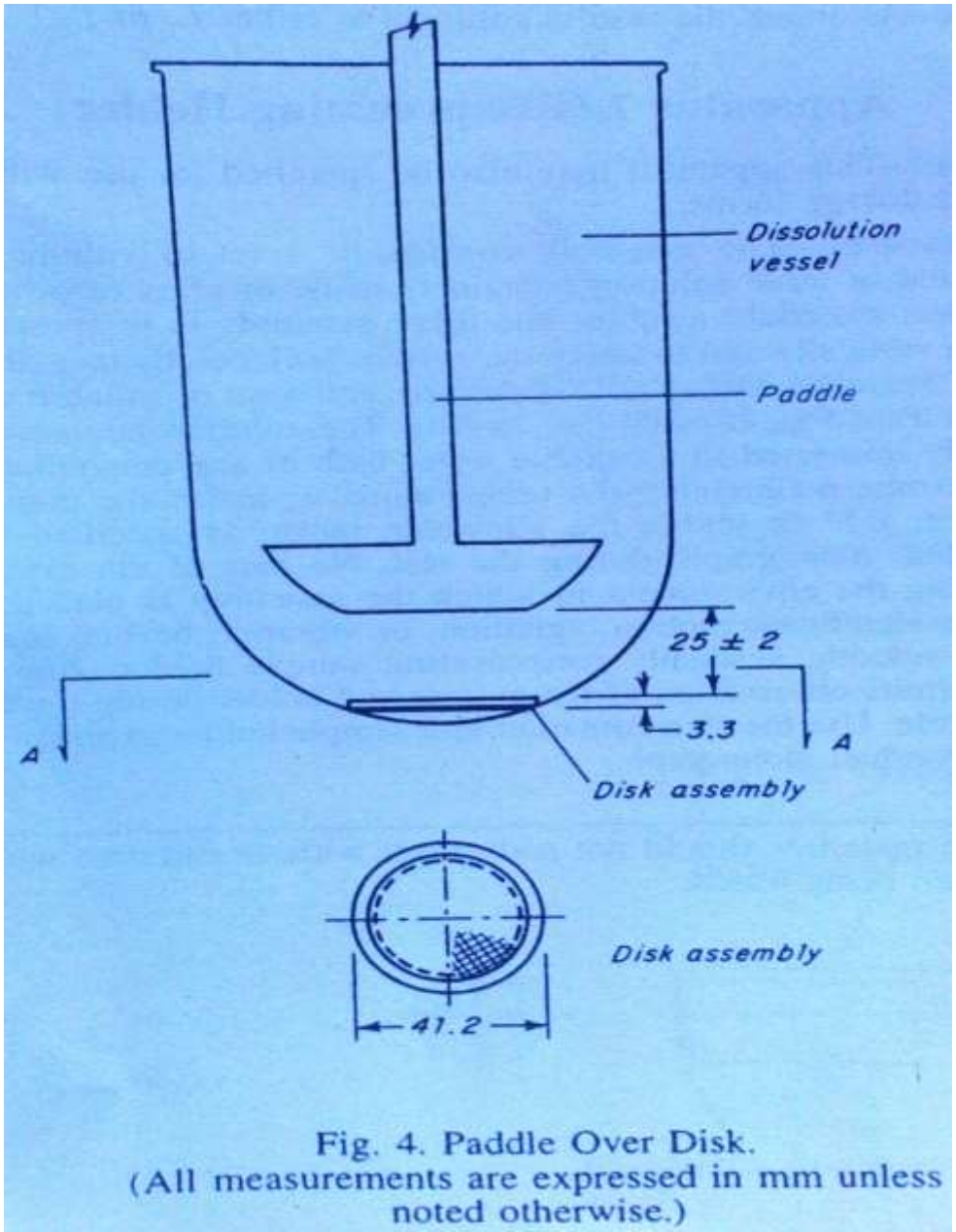


Fig. 4. Paddle Over Disk.
(All measurements are expressed in mm unless noted otherwise.)

CYLINDER METHOD (APPARATUS 6)

- Same as apparatus 1,except to replace the basket and shaft with a S.S. cylinder stirring element.
- Temperature - 32 ± 0.5°
- The dosage unit is placed on the cylinder.
- Distance between the inside bottom of the vessel and cylinder is maintained at 25 ± 2 mm.
- Used for transdermal formulation

RECIPROCATING HOLDER METHOD (APPARATUS 7)

- The assembly consists of a set of calibrated solution containers, a motor and drive assembly to reciprocate the system vertically.

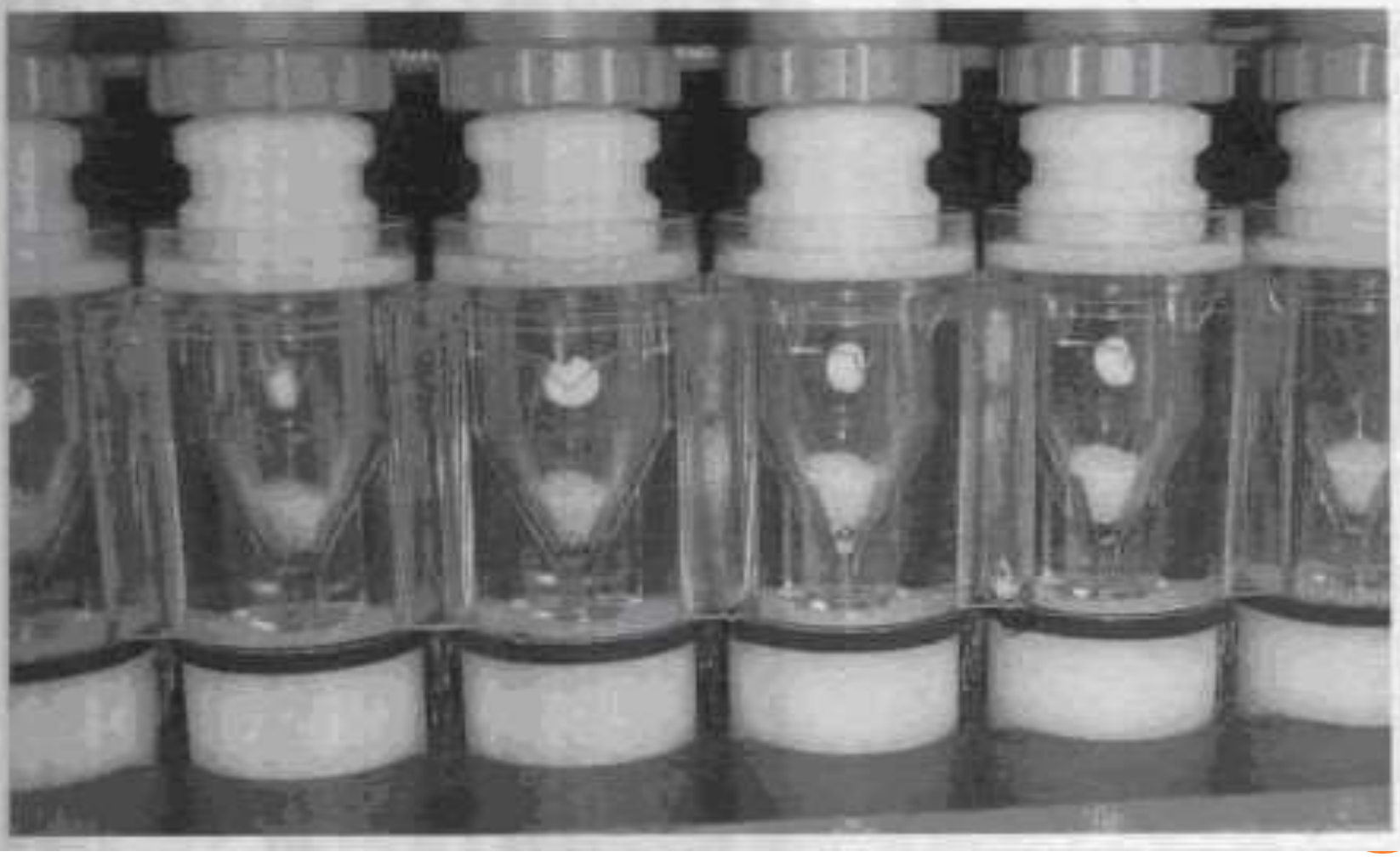
- Various type of sample holder are used.

- Used for controlled-release formulation

2. OPEN FLOW-THROUGH COMPARTMENT SYSTEM

- The dosage form is contained in a small vertical glass column with built in filter through which a continuous flow of the dissolution medium is circulated upward at a specific rate from an outside reservoir using a peristaltic or centrifugal pump.
- Dissolution fluid is collected in a separate reservoir.
- E.g. lipid filled soft Gelatin capsule

(d) Flow-through cell (USP IV).



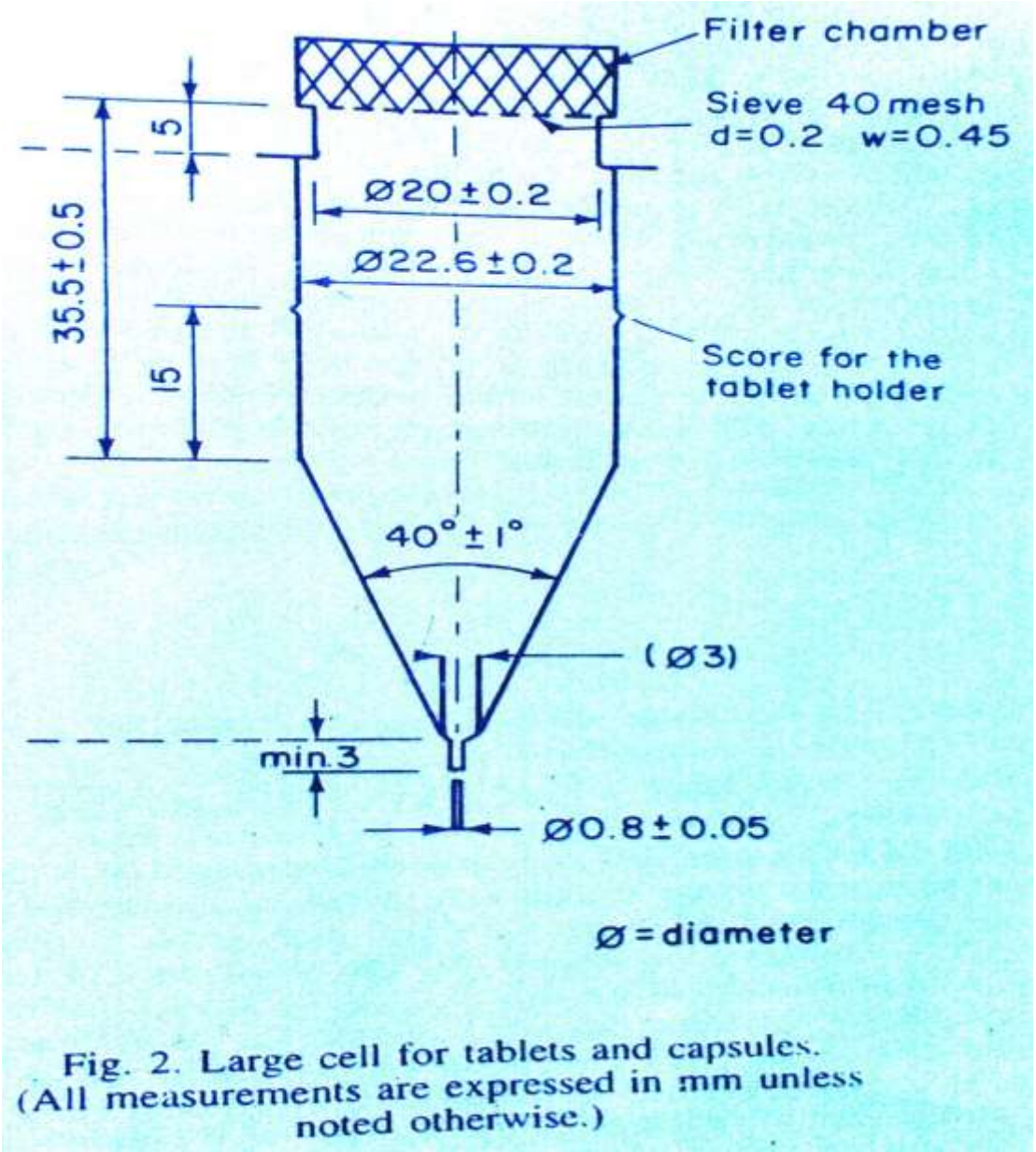


Fig. 2. Large cell for tablets and capsules. (All measurements are expressed in mm unless noted otherwise.)

⇨ ADVANTAGES

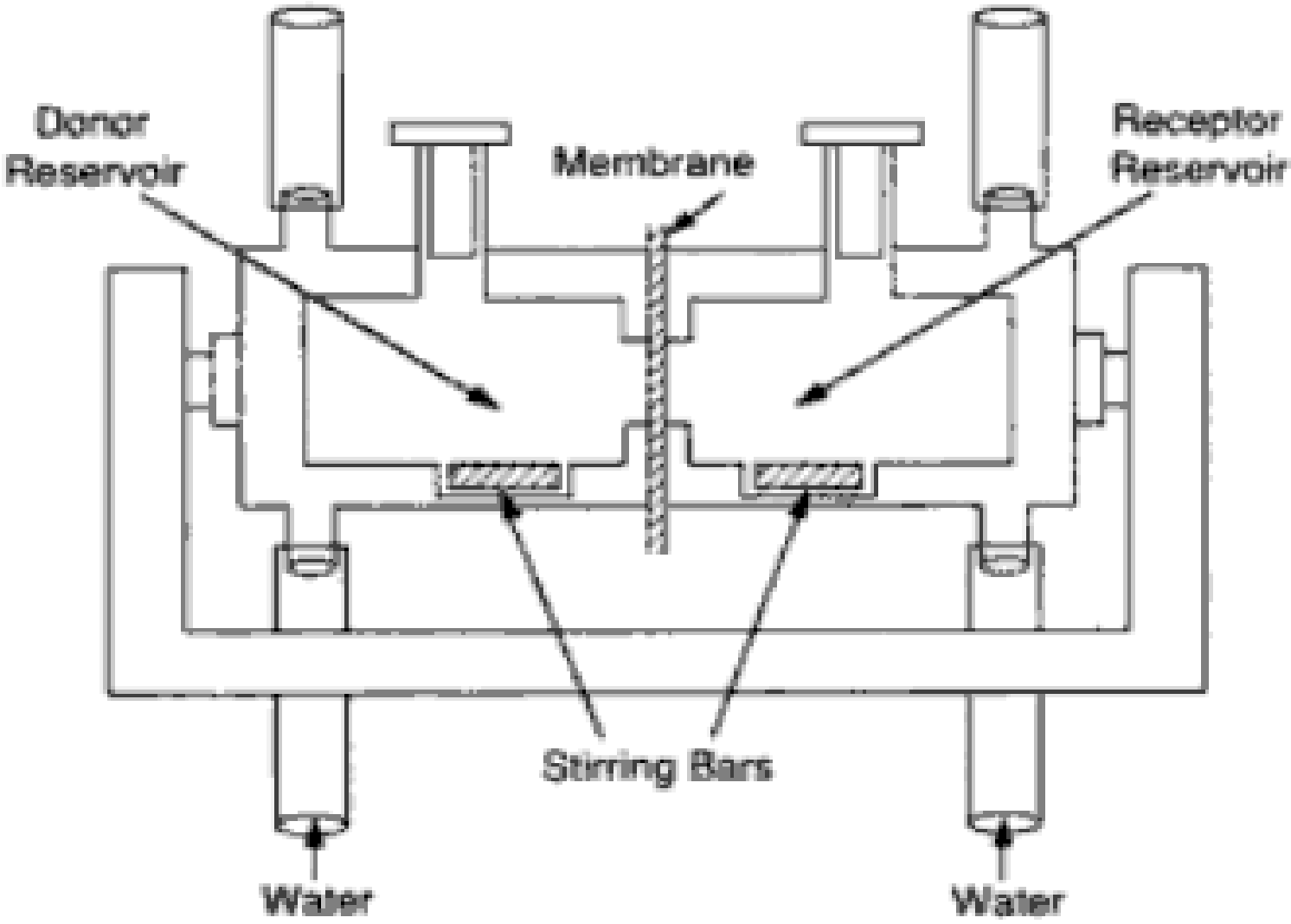
- No stirring and drug particles are exposed to homogeneous, laminar flow that can be precisely controlled. All the problems of wobbling, shaft eccentricity, vibration, stirrer position don't exist.
- There is no physical abrasion of solids.
- Perfect sink conditions can be maintained.

⇨ DISADVANTAGES

- Tendency of the filter to clog because of the unidirectional flow.
- Different types of pumps, such as peristaltic and centrifugal, have been shown to give different dissolution results.
- Temperature control is also much more difficult to achieve in column type flow through system than in the conventional stirred vessel type.

3. DIALYSIS SYSTEM

- Here, dialysis membrane used as a selective barrier between fresh solvent compartment and the cell compartment containing dosage form.
- It can be used in case of very poorly soluble drugs and dosage form such as ointments, creams and suspensions.


Donor
Reservoir
Membrane
Receptor
Reservoir
Stirring Bars
Water
Water

DISSOLUTION ACCEPTANCE CRITRIA

- **Q –Value –**

- Define as a percentage of drug content dissolved in a given time period.

DISSOLUTION ACCEPTANCE CRITRIA

STAGE	No. of Dosage units tested	Acceptance criteria
S1	6	No Dosage unit is less then Q+5%
S2	6	Average of 12 dosage units (S1+S2)>-Q% and no dosage unit is less then Q-15%
S3	12(6+6+12=24)	Average of 24 dosage units >-Q% And not more than two dosage units are less than Q-15% and No dosage unit is less than Q-25%

Thank you