Dissolution Test

Dissolution Test

1897 r. A.A. Noyes, W.R. Whitney (Massachusetts Institute of Technology)*

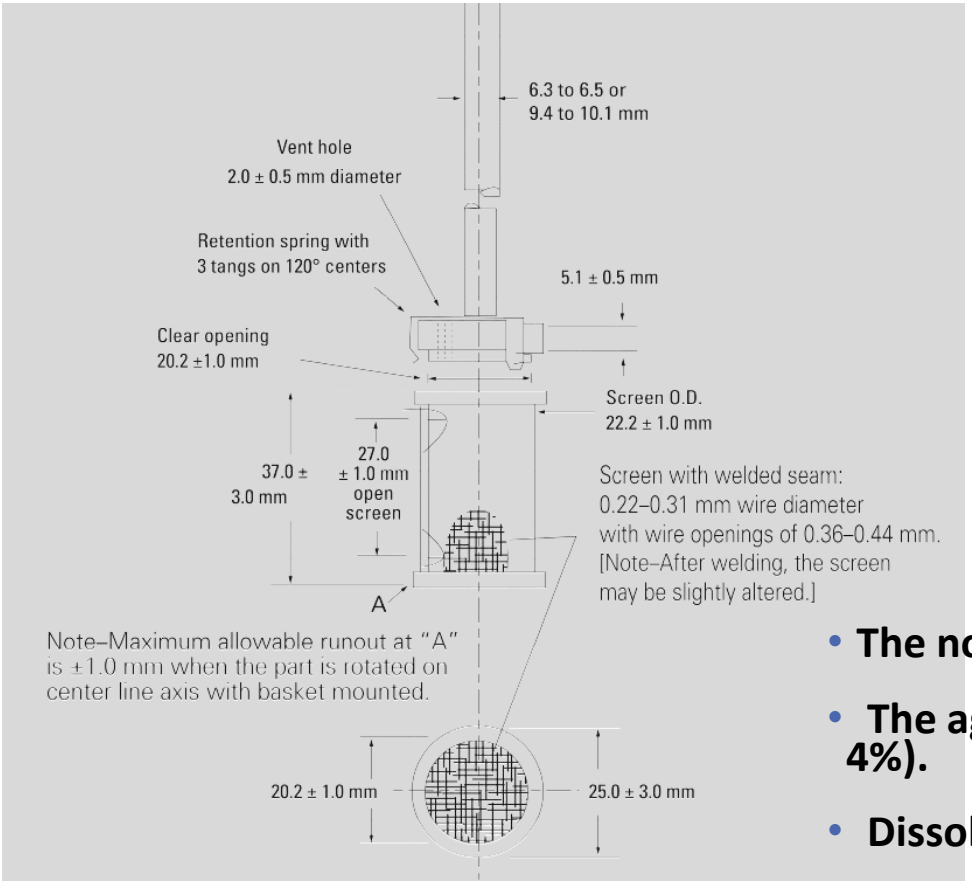
Dissolution testing measures the extent and rate of solution formation from a dosage form, such as tablet, capsule, ointment, etc. The **dissolution** of a drug is important for its bioavailability and therapeutic effectiveness. **Dissolution** and drug release are terms used interchangeably

- *N. Bou-Chacra et al., AAPS Journal, 2017.*

Dissolution Testing Apparatus

	USP 41-NF 36
Basket Apparatus (Rotate Basket)	Apparatus I
Paddle Apparatus	Apparatus II
Reciprocating Cylinder	Apparatus III
Flow-through Cell Apparatus	Appsratus IV
«Лопасть над диском»	Аппарат V
Rotate Cylinder	Apparatus VI
Reciprocating Holder	Apparatus VII

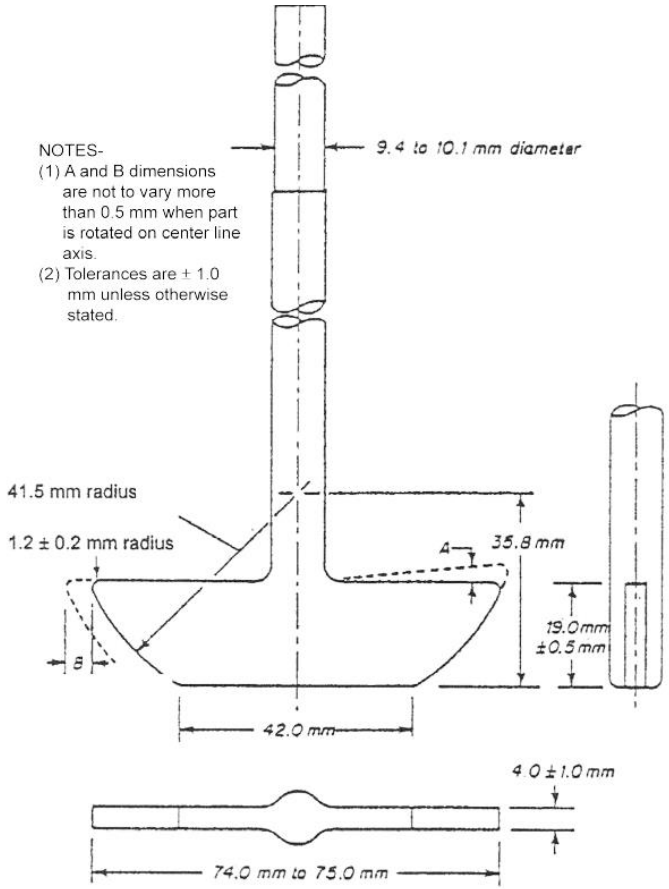
Apparatus I (Basket Apparatus)

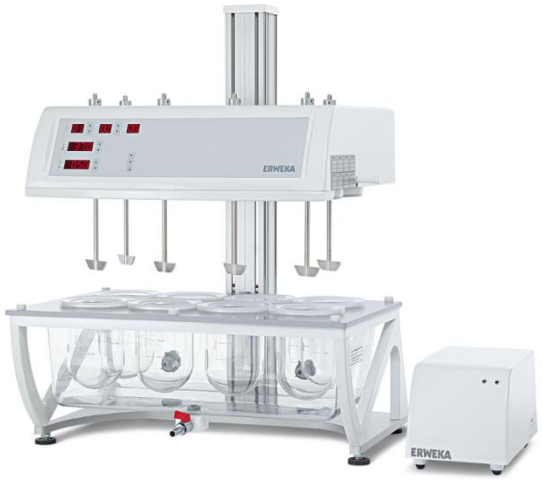


- **The nominal capacity of the vessel is 1000 ml.**
- **The agitator rotation speed is 100 rpm (tolerance ± 4%).**
- **Dissolution Medium Temperature is 37±0,5°C.**

USP 41-NF 36 General Chapter <711>

Apparatus II
(Paddle Apparatus)





- **The nominal capacity of the vessel is 1000 ml.**
- **The agitator rotation speed is 50 rpm (tolerance ± 4%).**
- **Dissolution Medium Temperature is 37±0,5°C.**

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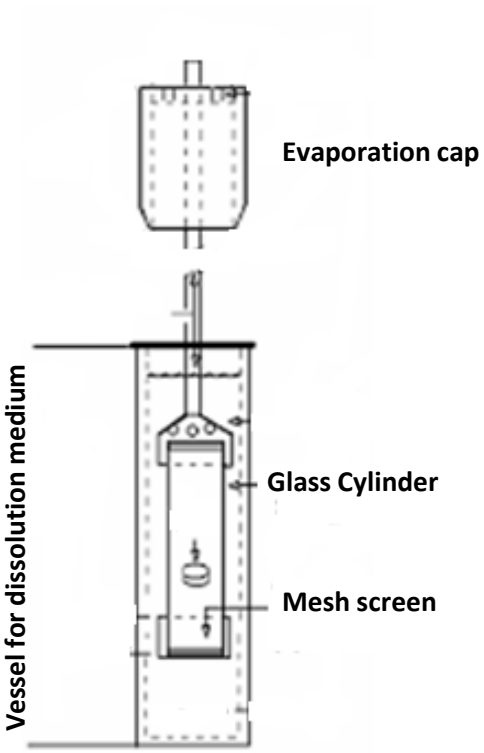
Apparatus III, VII Reciprocating Cylinder/Holder



It consists of a set of cylindrical flat-bottomed glass vessels, a set of glass piston cylinders. The cylinders make vertical reciprocating movements inside the vessels filled with the dissolution medium, the speed of the cylinders (the number of drops per minute) is indicated in the normative document.

Apparatus IV (Flow-Through Cell Apparatus)

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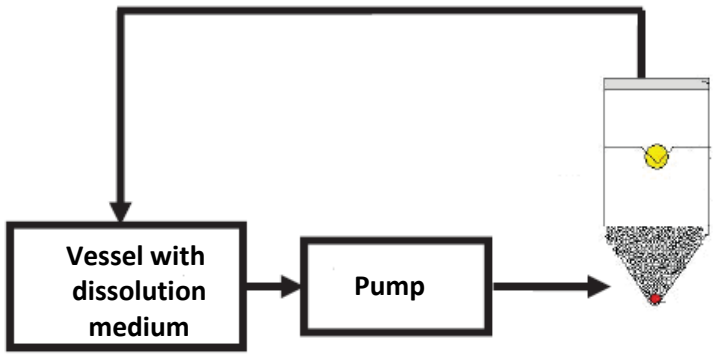
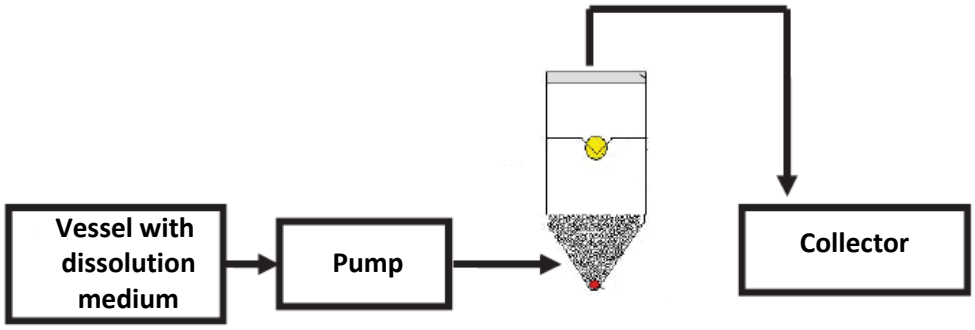


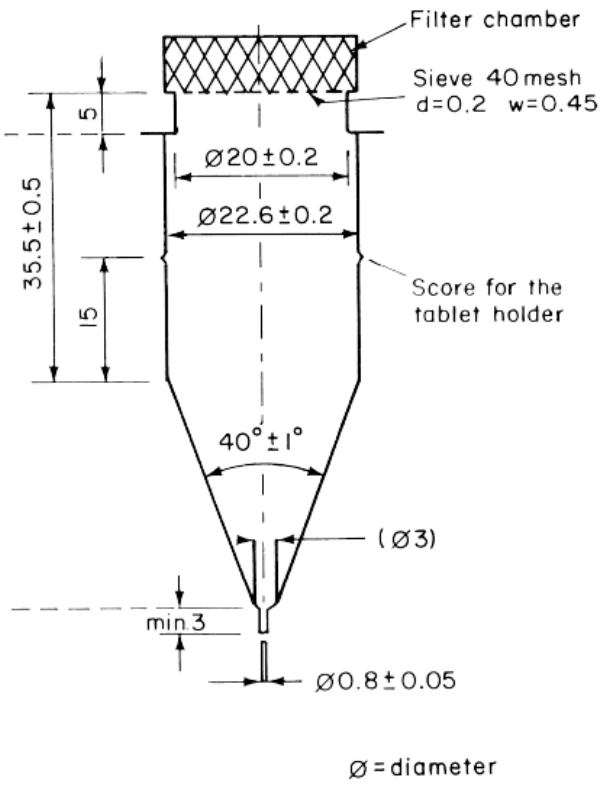
Closed mode



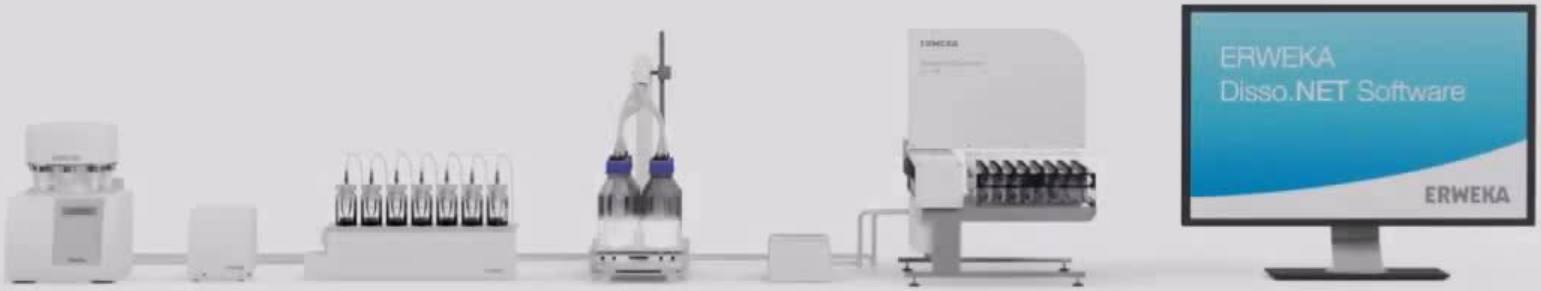
Open mode

* N. Fotaki, *Dissolution Technologies*, 2011.

Flow-Through Cell Apparatus



- **Pump with a sinusoidal velocity profile of 120 ± 10 pulses / min.**
- **The cell diameters are 12.0 and 22.6 mm.**
- **The flow rate of the medium should be indicated in specification (4, 8, 16 ml / min).**
- **The temperature of the dissolution medium is 37 ± 0.5 ° C.**



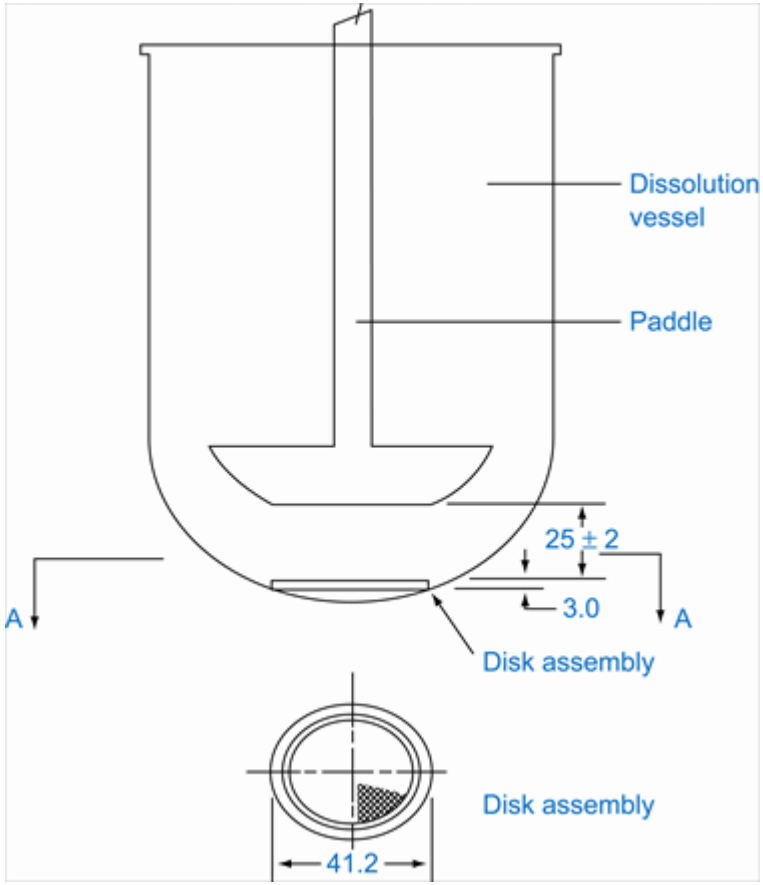
https://www.erweka.com/ru

Cell types


Tablet cell 12.00 mm
Tablet cell 22.6 mm
Granulate & Powder cell
Implant cell
Suppository cell
Stent cell
Tablet cell 22.6 mm with dialysis adapter
Tablet cell 22.6 mm with cream adapter
Tablet cell 22.6 mm with glass beads
Tablet cell 22.06 mm with glass beads

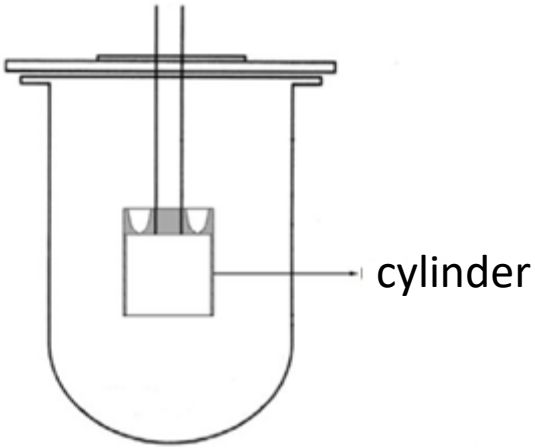

Glass beads 1 мм
Bead 5 мм

Apparatus V Paddle over Disk



The paddle mixer, additionally equipped with a stainless steel prefabricated disc in the form of a mesh with a hole size of 125 microns.

Apparatus VI (Rotating Cylinder)



The “paddle mixer” device, in which the rotating mixer and shaft are replaced by a rotating cylinder made of stainless steel.

Dissolution Test for Solid Dosage Forms

USP <711> Chapter

- **Immediate-release dosage forms**
- **Extended-release dosage forms**
- **Delayed-release dosage forms**

Noted in individual monograph

- Apparatus type;
- Dissolution medium (composition and volume);
- Rotation speed (apparatus I, II), medium flow rate (apparatus IV);
- Sampling time;
- Analytical method for quantitative determination;
- Requirements.

Dissolution media

- water;
- 0,1 M HCl;
- buffer solutions with pH 6,8-7,8 (allowed deviation pH ±0,05);
- other solutions that indicated in individual monograph;
- dissolved gases should be removed before testing.

Interpretation

Immediate-Release Dosage Forms

Stage	Number Tested	Acceptance Criteria
S_1	6	Each unit is not less than $Q + 5\%$.
S_2	6	Average of 12 units ($S_1 + S_2$) is equal to or greater than Q, and no unit is less than $Q - 15\%$.
S_3	12	Average of 24 units ($S_1 + S_2 + S_3$) is equal to or greater than Q, not more than 2 units are less than $Q - 15\%$, and no unit is less than $Q - 25\%$.

Interpretation

Extended-Release Dosage Forms

Level	Number Tested	Criteria
L_1	6	No individual value lies outside each of the stated ranges and no individual value is less than the stated amount at the final test time.
L_2	6	The average value of the 12 units ($L_1 + L_2$) lies within each of the stated ranges and is not less than the stated amount at the final test time; none is more than 10% of labeled content outside each of the stated ranges; and none is more than 10% of labeled content below the stated amount at the final test time.
L_3	12	The average value of the 24 units ($L_1 + L_2 + L_3$) lies within each of the stated ranges, and is not less than the stated amount at the final test time; not more than 2 of the 24 units are more than 10% of labeled content outside each of the stated ranges; not more than 2 of the 24 units are more than 10% of labeled content below the stated amount at the final test time; and none of the units is more than 20% of labeled content outside each of the stated ranges or more than 20% of labeled content below the stated amount at the final test time.

Interpretation

Delayed-Release Dosage Forms

- **Acid stage**

Level	Number Tested	Criteria
A_1	6	No individual value exceeds 10% dissolved.
A_2	6	Average of the 12 units ($A_1 + A_2$) is not more than 10% dissolved, and no individual unit is greater than 25% dissolved.
A_3	12	Average of the 24 units ($A_1 + A_2 + A_3$) is not more than 10% dissolved, and no individual unit is greater than 25% dissolved.

Interpretation

Delayed-Release Dosage Forms

- **Buffer stage**

Level	Number Tested	Criteria
B_1	6	Each unit is not less than Q + 5%.
B_2	6	Average of 12 units (B_1 + B_2) is equal to or greater than Q, and no unit is less than Q – 15%.
B_3	12	Average of 24 units (B_1 + B_2 + B_3) is equal to or greater than Q, not more than 2 units are less than Q – 15%, and no unit is less than Q – 25%.

Biorelevant media

1998 г. J. Dressman*

Biorelevant Media contain bile salts and lecithin to replicate fluids from different regions of the gut. They also represent both 'fasted' and 'fed' states. And even simulate fluids of different animal species. They can help you determine **biorelevant** solubility: how much drug product dissolves in the gut.

* J. Dressman et al., 1998, *Pharm. Research*

Biorelevant media simulated gastric fluid*

FaSSGF		FeSSGF	
Sodium thaurocholate	80 µM	Sodium chloride	237,02 мM
Lecithin	20 µM	Acetic acid	17,12 мM
Pepsin	0,1 mg/ml	Sodium acetate	29,75 мM
Sodium chloride	34,2 мM	Milk : buffer solution	1:1
Hydrochloric acid	qs pH 1,6	HCl/NaOH	qs pH 5,0
Deionized water	ad 1 L		

* E. Jantratid et al., 2008, *Pharm. Research*

Biorelevant media simulated intestine fluid*

FaSSIF-V2		FeSSIF-V2	
Sodium thaurocholate	3 мМ	Sodium thaurocholate	10 мМ
Lecithin	0,2 мМ	Lecithin	2 мМ
Maleic acid	19,12 мМ	Glyceril monooleate	5 мМ
Sodium hydroxide	34,8 мМ	Maleic acid	55,02 мМ
Sodium chloride	68,62 мМ	Sodium hydroxide	81,65 мМ
pH	6,5	Sodium chloride	125,5 мМ
		pH	5,8

* E. Jantratid et al., 2008, *Pharm. Research*

Biorelevant media simulated colon fluid*

FaSSCoF		FeSSCoF	
Tris(hydroxymethyl)-aminomethane	5,5 g	Tris(hydroxymethyl)-aminomethane	3,7 g
Maleic acid	8,8 g	Maleic acid	3,5 g
Sodium thaurocholate	0,0808 g	Bile salts extract	0,451 g
Lecithin solution (100mg/ml)	2,22 ml	Lecithin	0,370 g
Palmetic acid	0,026 g	Palmetic acid	0,051 g
Bovine serum albumin	3 g	Sodium chloride	2 g
Sodium hydroxide	ad pH 7,8 (1 L)	Glucose	14 g
		Bovine serum albumin	3 g
		Sodium hydroxide	ad pH 6,0 (1 L)

* M. Vertzoni et al., 2010, *Pharm. Research*

Application of Dissolution test

- drug development (selection of the optimal dosage form; evaluation of the properties of active substances);
- assessment of biopharmaceutical properties of medicines with modified and controlled release;
- assessment of bioequivalence of drugs;
- quality control of finished products