COLLEGE OF PHARMACY
UMM AL-QURA UNIVERSITY

Tablets Evaluation

Pharmaceutics III
Lecture 5

Learning Objectives

By the end of this lecture, the student will be able to:

1. State quality standards and USP compendial requirements for tablets.
2. Discuss the differences between official and non-official tests.
3. Categorize types of tablet evaluation tests based on USP officiality.
4. Describe appropriate techniques to run each analysis.
5. Explain the various factors affecting the results of quality control tests.

The Importance of Quality Control Testing

- Quality control is an important requirement to ensure the suitability of the products for use, sale or supply.
- It is concerned with sampling, specification, and testing the products to according to highly standardized procedures.
- Quality control tests are performed on each batch and the results are documented and examined by experts before releasing the products.

Quality Control Testing of Tablets

OFFICIAL TESTS

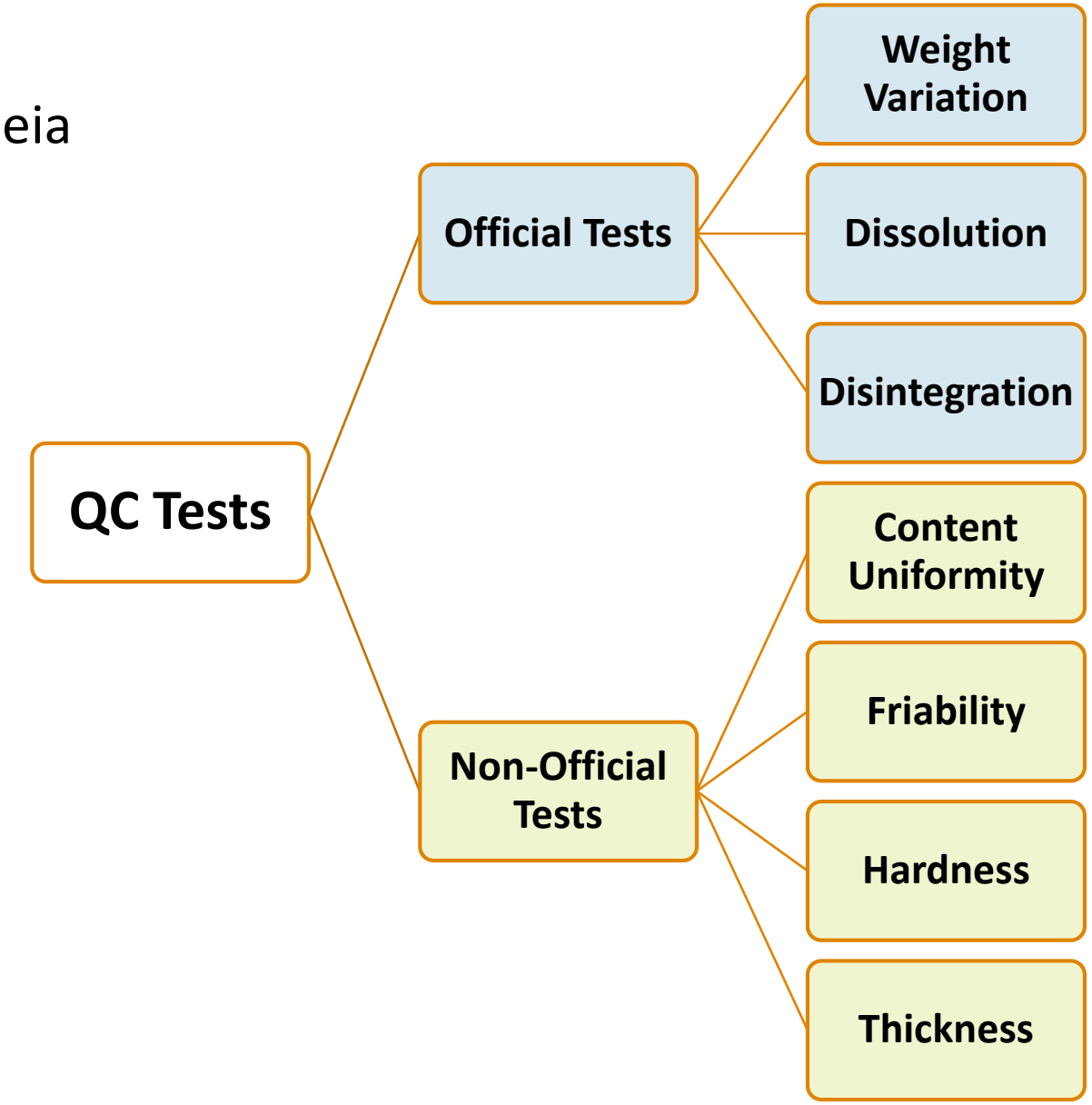
- They are called official tests because the test methods are described in official compendia.
- They are standardized test procedures that clearly stated limits under which tablets are accepted.
- These tests are concerned with the content and the *in vitro* release of the active ingredients.

NON-OFFICIAL TESTS

- These are tests that are performed on tablets and which are not listed in official compendia.
- They are concerned a variety of quality attributes that need to be evaluated, such as hardness or friability test, or thickness test etc.
- Some of these tests have no officially set limits for acceptance or rejection and thus may vary from manufacturer to manufacturer and from formulation to formulation.

Quality Control Testing of Tablets

- US pharmacopeia classified QC testing into:



Official Tests
1. Weight Variation Test

- Tablets generally are manufactured to contain a certain amount of active ingredients in a certain weight of tablet.
- In this test, samples of 20 tablets are removed from a batch from time to time during compression, and then are weighed to determine whether they conform to the required weight criteria.
- There still may be a difference in the individual weights even when 20 tablets show the expected total weight.

Official Tests
1. Weight Variation Test

- Twenty tablets are weighed individually.
- Individual weights are compared with the average weight. If no more than two tablets are outside the percentage limit, and if no tablet differs by more than two times the percentage limit, the tablets pass the USP weight variation tests.

Average Weight of Tablet (mg)	Maximum (%) Weight Difference Allowed
130 or less	10
130–324	7.5
More than 324	5.0

Official Tests
1. Weight Variation Test

❑ **If the drug occupies the <u>greater part</u> of the tablet mass:**

Any weight variation reflects variations in the content of active ingredient.

❑ **In case of potent drugs:**

The excipients form **<u>the greater</u>** part of the tablet weight & so the relationship between tablet weight and amount of active ingredient is poor.

Official Tests
1. Weight Variation Test

Causes of weight variation:

- ❑ Differences in the size of the compressed granules (presence of too large or too fine granules).
- ❑ Poor flow (causes incomplete filling of the die).
- ❑ Poor mixing (due to non-even distribution of the lubricants & glidants).
- ❑ Unequal length of lower punches causes different filling of each die.

Official Tests
2. Content Uniformity Test

- Determines the amount of drug in a sample of tablets.
- For tablets in which the active ingredients make up about 90% of the tablet weight, the weight variation test will give a good measure of content uniformity.
- The acceptable potency range for **low-dose, highly potent drugs** is **90%-110%.**
- For **large-dose drugs**, the range is **95%-105%** of the labelled amount.
- No tablet should fall in the range of **75 – 125% deviation** (tablets then classified as under-doses or over-dosed).

Official Tests
2. Content Uniformity Test

- Select 30 tablets randomly from a batch. Assay 10 tablets individually.
- Nine of them must contain not less than 85% or more than 115% of the labeled drug content.
- The tenth tablet may not contain less than 75% or more than 125% of the labeled drug content.
- If the preceding conditions are not met, the 30 remaining tablets are assayed individually and none may fall outside the 85%115% range.
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Official Tests
2. Content Uniformity Test

Causes of content uniformity:

- ❑ Nonuniform distribution of the drug in the powder or granules.
- ❑ Segregation of the powder mixture or granulation during manufacturing processes.
- ❑ Tablet weight variation.

Official Tests
3. Disintegration Test

- The first thing that happens to a tablet before absorption is disintegration, or breaking down of the tablets to granules and powders before dissolving in the gastric fluid.
- For absorption to take place, dissolution of the drug in the gastrointestinal fluid has to occur, since only the drug in solution is absorbed.

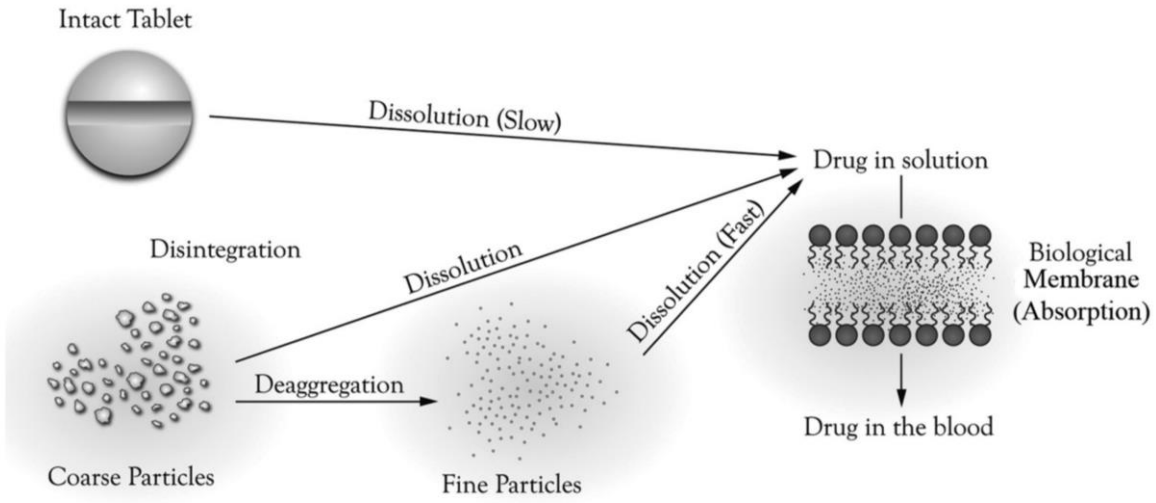


FIGURE 8.4 Absorption of a drug from an intact tablet.

Official Tests
3. Disintegration Test

- The time it takes to disintegrate is called disintegration time and is measured by a USP disintegration apparatus.
- The USP disintegration apparatus uses six tubes open at both ends with a 10-mesh screen at the bottom of the tube. Baskets are reciprocated up and down a certain distance at a frequency of 28-32 cycles per minute.
- The medium can be water or simulated gastric or intestinal fluid, and the volume of the medium is 1000 mL. The temperature is 37± 2 °C.

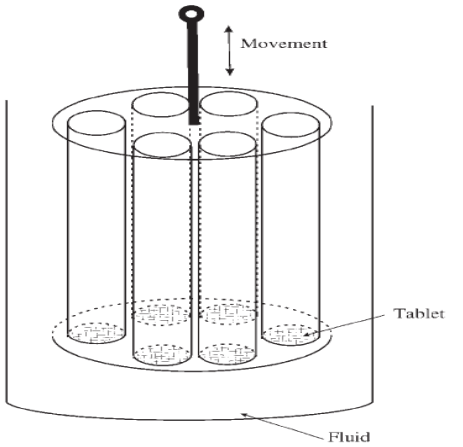


Fig. 2 Schematic of a tablet disintegration apparatus.

Official Tests
3. Disintegration Test

- The tablet must disintegrate and all particles pass through to 10-mesh screen in the specified time.
- For immediate-release tablets, the disintegration time should be within 5-30 minutes.
- For enteric-coated tablets, no disintegration should occur within 1 hour in simulated gastric fluid, but the same tablets have to disintegrate in 2 hours plus the time stated in the USP monograph when they are placed in simulated intestinal fluid.

Official Tests
3. Disintegration Test

- **Factors affecting the disintegration time include:** media and the temperature of the disintegration test media, the nature of the drug, the diluent used in the formulation, the type and amount of binder and disintegrant used.

Official Tests
3. Disintegration Test

The objectives of a dissolution study are:

- ❑ To ensure that the drug is completely released or close to 100% release from the tablet.
- ❑ The rate of drug release is uniform from batch to batch.
- ❑ The release is same as the release rate from batches proven to be bioavailable and clinically effective.

Official Tests
3. Disintegration Test

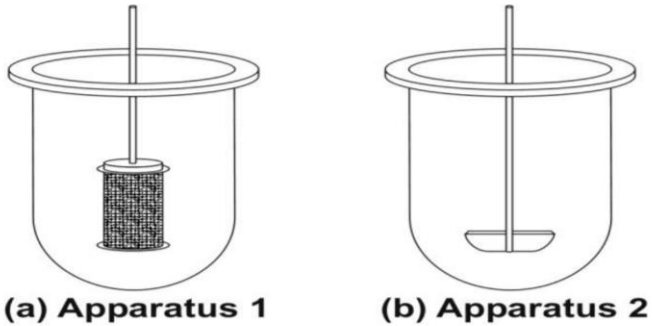
- The rate at which a solid dissolves in a solvent is given by the Noyes and Whitney (1897) equation:

$$\frac{dc}{dt} = \frac{DA}{Vh}(C_s - C)$$

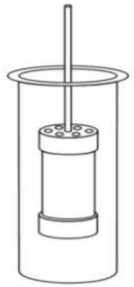
where dc/dt is the dissolution rate, D is the diffusion coefficient of the solute in dissolution medium, A is the surface area of the exposed solid, h is the thickness of the diffusion layer, C_s is the solubility of the solid in the dissolution medium, C is the concentration of the solute at any time t, and V is the volume of the release medium.

- There are many dissolution apparatuses used to determine the dissolution profiles of drugs from different dosage forms.
- USP Apparatus #1 (rotating basket) and USP Apparatus #2 (paddle method) are commonly used to evaluate the dissolution profile of solid dosage forms.

Official Tests
3. Disintegration Test

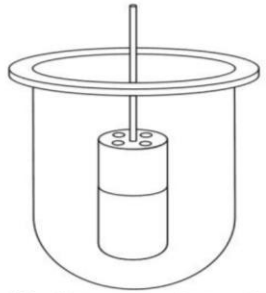

(a) Apparatus 1

(b) Apparatus 2


(c) Apparatus 3


(d) Apparatus 4


(e) Apparatus 5


(f) Apparatus 6

Schematic representation of official USP dissolution apparatus:

a. Apparatus 1: rotating basket apparatus.
b. Apparatus 2: rotating paddle apparatus.
c. Apparatus 3: reciprocating cylinder apparatus.
d. Apparatus 4: flow through cell apparatus.
e. Apparatus 5: paddle over disc apparatus.
f. Apparatus 6: cylinder apparatus.

Official Tests
3. Disintegration Test

- The amount of drug dissolved within a certain time period is determined by taking samples from the dissolution medium and analyzed after specified time intervals.
- **Limit:** 75% of the drug should be dissolved within 30 minutes, unless otherwise specified by the manufacturer.
- First, the dissolution of six tablets is tested and accepted if all six tablets are not less than the USP monograph tolerance limit plus 5%.
- If they fail, another number of tablets will be tested for a couple of times under different tolerance limits.
- Dissolution results are plotted as concentration versus time.

Official Tests
3. Disintegration Test

TABLE 8.6 Comparison of Different USP Dissolution Apparatuses

USP Apparatus	Description of the Apparatus	Rotation Speed	Dosage Forms to be Tested
I	Basket	50–120 rpm	Immediate-release tablets Delayed-release tablets Extended-release tablets
II	Paddle	25–50 rpm	Immediate-release tablets Delayed-release tablets Extended-release tablets
III	Reciprocating cylinder	6–35 dpm (dips per minute)	Immediate-release tablets Extended-release tablets
IV	Flow-through cells	N/A	Extended-release tablets Poorly soluble drug
V	Paddle over disk	25–50 rpm	Transdermal
VI	Cylinder	N/A	Transdermal
VII	Reciprocating disk	30 rpm	Extended-release tablets

USP dissolution conditions are maintained as close as possible to the *in vivo* situation:

Temperature:	37° ± 0.5°C
Medium:	0.1 N HCl, pH 7.4 buffer
	Simulated gastric fluid
	Simulated intestinal fluid, water
Agitation:	Mild
Volume of the Medium:	Enough to maintain sink condition (1000 mL)

Dissolution Test-How does it work?

Un-Official Tests
1. General Inspection

- Visual inspection and identification for any flaws that may affect the appearance.

Reasons for general inspection:

- To control and check batch to batch uniformity.
- To control any manufacturing issues.
- To ensure consumer acceptance.

Inspection includes:

- Tablet size, shape, color, odor, any physical flaws ..etc..

Un-Official Tests
2. Hardness Test

- Hardness is generally expressed as the force required to break a tablet in a diametric compression test; it is often called breaking strength or tablet crushing strength.

Reasons for tablets to require a certain amount of strength or hardness:

- To withstand mechanical shocks of handling during manufacture, packaging and shipping.
- The relationship of hardness to tablet disintegration and dissolution (relating mechanical strength to disintegration and dissolution).

Test Description:

- A tablet is placed between two anvils, force is applied to the anvils, & the crushing strength that just causes the tablet to break is recorded (in kg).
- Tablet hardness should be between 6 – 10 kg.

Un-Official Tests
2. Hardness Test

- Tablet hardness depends on compression load. Hardness increases with an increase in pressure, as this causes the tablet to laminate or cap.
- **Hardness depends on:** compression force, concentration and type of binding agent.
- If the tablet initially is too hard, it may not disintegrate in the requested period of time.
- If it is too soft, it may not withstand the necessary multiple shocks occurring during handling, shipping, and dispensing.

Un-Official Tests
2. Hardness Test

- Lozenges and buccal tablets are intended to dissolve slowly, so they are prepared to be hard.
- Some immediate-drug release tablets or soluble tablets are made to be soft (not too hard) to break and disintegrate easily.
- Hardness generally increase with normal storage of tablets.

Hardness Test-How does it work?

Un-Official Tests
3. Thickness Test

- The thickness of a tablet is determined by: the diameter of the die, the compaction characteristics of the fill material, and the force or pressure applied during compression.
- The thickness of individual tablets can be measured with a micrometer.
- Thickness should be within ± 5% variation of a standard value.
- Tablet thickness becomes very important in packing operations.

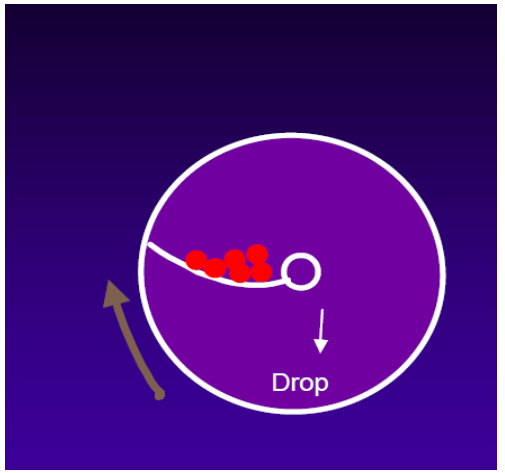
Un-Official Tests
4. Friability Test

- Friability is a measure of the tendency of a tablet to powder, chip, and fragment during handling and is another measure of tablet strength.
- A Roche friabilator is used to measure the friability of a tablet.
- A pre-weighed tablet sample is placed in the friabilator and dropped over a distance during each rotation and operated for 4 minutes (100 rotations). The tablets are dusted and reweighed.
- Accepted tablets are those that do not lose more than 0.5%1.0% of their weight.

Un-Official Tests
4. Friability Test

- The friability of tablets may be influenced by moisture content.
- Chewable tablets show a high friability weight loss compared to conventional compressed tablets.

Friabilator-How does it work?



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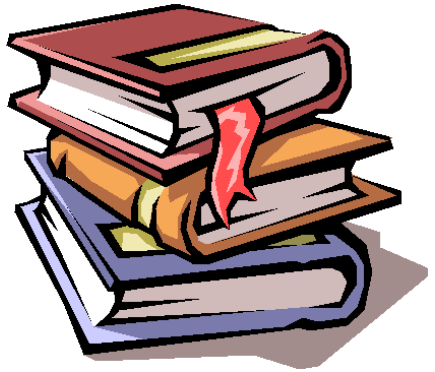

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