

In-process Quality Control :

1. Diameter
2. Thickness
3. Weight variation
4. Hardness
5. Friability
6. Disintegration time

Report :**QUESTION BANK**

1. Wet granulation (water based) is not suitable to manufacture of aspirin tablets. Why?
2. Draw a flow-chart for the production of aspirin tablets.
3. Name a few drugs suitable for the manufacture of tablets by direct compression methods.
4. What are the criteria for the selection of a drug for direct compression technique?
5. List the advantages of direct compression method.
6. List a few examples of directly compressible vehicles and give their compaction properties.

In-process Quality Control Tests for Uncoated Tablets

Experiment No. 6

Date :

Aim : To evaluate uncoated tablets for in-process quality control tests.

Theory

A variety of tests are conducted on tablets in order to make sure that the manufactured tablets are of the best possible quality. From the point of production of tablets, quality control tests are classified into two categories.

<i>In-process quality control tests</i>	<i>Finished product quality assurance tests</i>
Appearance	Dissolution rate
Dimensions	Uniformity of content
Uniformity of weight (Weight variation)	Content of active ingredient and confirmation of all the tests reported in in-process quality control
Hardness	
Friability	
Disintegration time	

In-process Quality Control Tests

In-process quality control tests are the tests conducted when the tableting is under process. These tests should be completed quickly, without halting the process for long time. In this experiment, in-process quality control tests are performed on uncoated tablets.

Finished product quality control tests are performed after completion of compression. They are not performed in the production department. However theory related to these tests is explained.

Appearance (unofficial test) : The tablets should be free from cracks, depressions, pinholes, etc. The colour and polish of the tablet should be uniform on whole surface. There should be no signs of coating. The surface of the tablets should be smooth.

Dimensions (unofficial test) : The dimensions of the tablets are thickness and diameter. The tablets should have uniform thickness and diameter. These are normally stated by the manufacturer. Thickness and diameter of a tablet are measured using a vernier calipers or screw gauge. These values are checked and are used to adjust the initial stages of compression. These dimensions are related to hardness and friability.

Uniformity of weight (weight variation test) (official test) : This is an important in-process quality control test to be checked frequently (every half an hour). Corrections are made during the compression of tablets if necessary. Any variation in the weight of tablet (for any reason) leads to either under medication or overdose. This is particularly true when the drugs are potent or low-dose drugs. All tablet machines have provision to receive a known quantity (volume which is correlated to weight) of granules.

The tolerance values of weight variation for uncoated tablets as per IP are as shown in the table.

Average weight (mg)	Percentage deviation
80 or less	10.0
More than 80 and less than 250	7.5
250 or more	5.0

Improper flow of granules from hopper into the die is responsible for weight variation. Lubricants (magnesium stearate), glidants (corn starch, talc), and antiadherants (talc, corn starch) are added for the proper flow of granules. Optimum amount of fines also improves the flow and helps to maintain uniform weight of tablet.

Hardness (unofficial test) : Hardness (diametral crushing strength) is a force required to break a tablet across the diameter.

The hardness of a tablet is an indication of its strength. The tablet should be stable to mechanical stress during handling and transportation. The degree of hardness varies with the different manufacturers and with the different types of tablets. The force is measured in kilograms and the hardness of about 4 kg is considered to be satisfactory for uncoated tablet. It is tested by using hardness testers such as Monsanto tester (Figure 4), Pfizer tester (Figure-5), Erweka tester, Schleuniger tester, and Strong-Cobb tester. Unfortunately, different testers do not produce the same results for the tablet.

This is a valuable test, which might influence tablet disintegration and dissolution rate. Depending on the type and concentration of the

binding agent (for example, acacia mucilage, starch paste, sugar syrup, methyl cellulose dispersion etc), the hardness of the tablet varies. For each product, the manufacturer prescribes the degree of hardness.

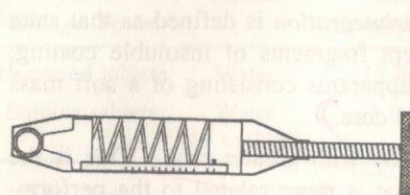


Figure 4. Monsanto hardness tester.

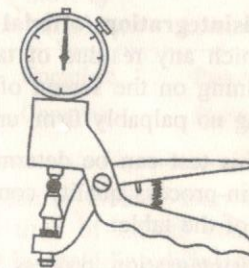


Figure 5. Pfizer hardness tester.

Friability (unofficial test) : Friability is the loss of weight of tablet in the container/package, due to removal of fine particles from the surface.

This in-process quality control test is performed to ensure the ability of tablets to withstand the shocks during processing (coating and strip-packing), handling, transportation, and shipment. The friability of tablets is indicated by chipping, capping, or breaking.

The extent of friability is estimated using Roche friabilator (Figure 6). It is expressed as percentage w/w. The allowable friability is less than 0.8%. This limit is strictly adhered when the tablets are further processed for coating.

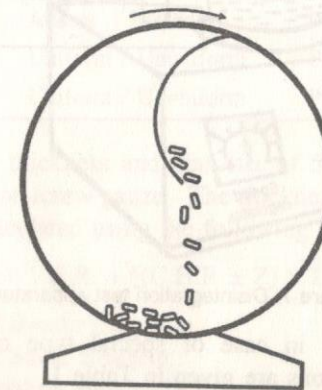


Figure 6. Roche friabilator.

Friability problems are encountered with thin-tablets, large-diameter tablets, granules having excessive fines (due to entrapped air), or excessively dried granules.

Disintegration (official test) : *Disintegration* is defined as that state in which any residue of tablet, except fragments of insoluble coating, remaining on the screen of the test apparatus consisting of a soft mass having no palpably firm, unmoistened core.

This test can be determined quickly with greater ease. This is the only in-process quality control test that is more related to the performance of the tablet.

Disintegration process involves the breaking of tablet into small particles. The quicker the disintegration, the faster could be the action. Disintegration roughly indicates the possible pattern of dissolution of active substance. Hence, the experimental conditions closely mimic the situations that a tablet encounters in gastrointestinal tract, in terms of temperature, pH and mechanics. For this purpose, the pharmacopoeia prescribed specifications and standards for equipment and procedures (Figure 7). The disintegration time should be as less as possible unless

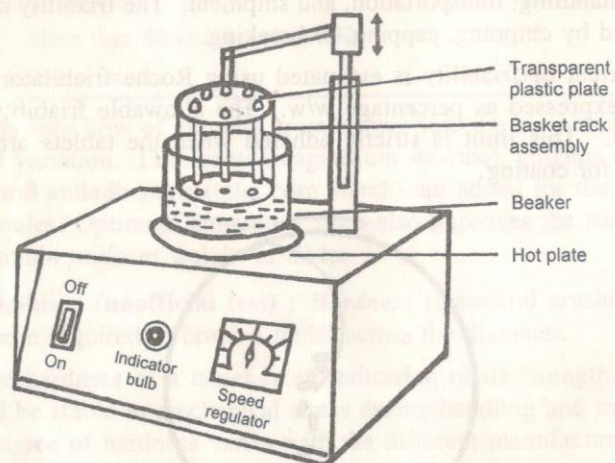


Figure 7. Disintegration test apparatus.

otherwise specified as in case of special type of controlled release products. IP specifications are given in Table 1.

TABLE I
Specifications for Disintegration for Tablets

Type of dosage Form	Vehicle	Time of disintegration	State of disintegration	Remarks
Uncoated tablets	Water	15 min.	Complete	Passes
Soluble tablets	Water (19 to 21°C)	3 min.	Complete	Passes

This test is not applicable to sustained release tablets, chewable tablets, and sublingual tablets. Disintegration time of tablets can be reduced (or disintegration rate can be enhanced) by including disintegrating agents such as starch, methylcellulose, etc., in the formulation.

Procedure

The procedures for in-process quality control tests are explained below.

Appearance : The tablets are examined externally under a biconvex lens for surface, colour, polish, etc. The tablets should be free from cracks, depressions, pinholes, etc.

Test	Observation	Inference
Surface roughness	Smooth / Irregular	Passes / Does not pass
Cracks	Absent / Present	Passes / Does not pass
Depressions	Absent / Present	Passes / Does not pass
Pinholes	Absent / Present	Passes / Does not pass
Colour	Uniform / Ununiform	Passes / Does not pass
Polish	Uniform / Ununiform	Passes / Does not pass

Dimensions : The thickness and diameter of 5 tablets are measured using vernier calipers or screw gauge. The thickness and diameter of the tablet is accurately calculated using the following formula.

$$T.R. = P.S.R. + [(C.H.R \pm Z) \times L.C.]$$

where, T.R. = Total Reading
P.S.R. = Pitch Scale Reading
C.H.R. = Coinciding Headscale Reading
L.C. = Least Count
Z = Zero correction

Tablet no.	Weight of a tablet, mg	Average weight, mg	Difference, mg	Per cent difference	More / less than official limit
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					
16					
17					
18					
19					
20					

Per cent difference =
 Number of tablets falling beyond the official limit :
 Batch of tablets passes / does not pass for weight variation test.

Uniformity of weight (weight variation) : Every tablet in each batch should have a uniform weight. 20 tablets are weighed individually. Average weight is calculated from the total weight of all tablets. The individual weights are compared with the average weight. The percentage difference in the weight variation should be within the permissible limits (given in earlier sections).

The percentage deviation is calculated by using the following formula.

$$\text{Per cent deviation} = \frac{\text{individual weight} - \text{average weight}}{\text{average weight}} \times 100$$

Hardness (The hardness of tablet is tested using the hardness tester (Figure 4). The tablet is placed across the diameter in between the spindle and the anvil. The knob is adjusted to hold the tablet in position. The reading of the pointer is adjusted to zero. The pressure is increased slowly to break the tablet.) "Hardness factor" - the average of the several determinations is determined and reported.

Sl. no.	Hardness, kg/cm ²
1	
2	
3	
4	
5	

Average hardness of tablets:kg / cm².
 Batch of tablets passes/does not pass for hardness test.

Friability (Roche friabilator is used to measure the friability of the tablets (Figure 5). It rotates at a rate of 25 rpm. 10 tablets are weighed collectively and placed in the chamber of the friabilator. In the friabilator, the tablets are exposed to rolling, resulting from free fall of tablets within the chamber of the friabilator. After 100 rotations (4 minutes), the tablets are taken out from the friabilator and intact tablets are again weighed collectively. Percentage friability is determined using the following formula.

$$\% \text{ Friability} = \frac{(W_1 - W_2)}{W_1} \times 100$$

where W_1 = Weight of the tablets before test
 W_2 = Weight of the tablets after test

Weight of 10 tablets, g		Difference ($W_1 - W_2$), g	% Friability
Before test, W_1 g	After test, W_2 g		

Permitted percent friability = 0.8

Batch of tablets passes / does not pass for friability test.

Disintegration : The disintegration test apparatus consists of a basket-rack assembly containing six open-ended glass tubes (Figure 7). They are held vertically and the bottom of the tube is covered with 10-mesh screen. By the use of a motor, the basket raises and lowers in the immersion fluid at a frequency of 29 to 32 cycles per minute. The wire screen is always maintained below the level of the fluid. The fluid temperature is maintained at $37 \pm 2^\circ\text{C}$ throughout the test.

The sinker provides the necessary impact on the tablet under motion. The procedure is given in the table below. The disintegration time is noted when all tablets pass through the sieve. This time should comply with the time stated in the monograph for that tablet.

Test	Observation	Inference
Water (or specified medium) is placed in the disintegration apparatus. The temperature of the medium is maintained 37°C . A tablet is placed in each of the six tubes of the basket. Then the plastic discs (weights) are placed over each tablet to prevent the tablet coming outside of the tubes of the basket. The basket is allowed to operate.	Time required for complete disintegration of all the six tablets is min	Batch of tablets passes / does not pass for disintegration test

Disintegration time for uncoated tablets (unless stated in IP) is 15 minutes.

Batch of tablets passes / does not pass for disintegration test.

Summary of Observations

Sl. No.	Test	Observation	Inference
1	Appearance		
2	Tablet thickness		
3	Tablet diameter		
4	Uniformity of weight		
5	Hardness		
6	Friability		
7	Disintegration		

Report :

QUESTION BANK

1. Enumerate official quality control tests for uncoated tablets.
2. How are in-process quality control tests different from finished product quality control tests?
3. A particular tablet has not passed the friability test. What are the types of problems foreseen in the market place?

