**Quality Control of Tablets**

Compressed tablets may be characterized or described by a number of specifications. These include: shape, diameter, thickness, weight, hardness, friability, disintegration time and dissolution characteristics.

**Diameter and shape:**

* The diameter and shape depend on the die and punches selected for the compression of the tablet.
* Generally, tablets are discoid in shape, although they may be oval, oblong, round, cylindrical, or triangular.
* Their upper and lower surfaces may be flat, round, concave or convex to various degrees.
* The tablets may be scored in halves or quadrantsto facilitate breaking if smaller dose is desired.
* The top or lower surface may be embossed or engraved with a symbol or letters which serve as an additional mean of identifying the source of the tablets.
* These characteristics along with the color of the tablets tend to make them distinctive and identifiable with the active ingredient which they contain.

**Tablet thickness:**

The thickness of the tablet is the only dimensional variable related to the compression process. Tablet thickness is consistent batch to batch or within a batch only if the tablet granulation or powder blend is adequetly consistent in particle size and size distribution, if the punch tooling is of consistent length , and if the tablet press is clean and in good working order.

* The thickness of individual tablets may be measured with a micrometer.
* Thickness should be controlled within ± 5% variation of a standard value.
* Thickness must be controlled for consumer acceptance of the product, and to facilitate packaging.

**Organoleptic properties (color, odor and taste):**

**Color:**

* Many pharmaceutical tablets use color as a vital means of rapid identification and consumer acceptance.
* The color of a product must be uniform within a single tablet (uniformity is referred to as ‘mottling’).
* Nonuniformity of coloring not only lacks esthetic appeal but could be associated with poor quality of the product.

**Odor:**

* The presence of odor in a batch of tablets could indicate stability problems, such as the odor of acetic acid in degrading aspirin tablets.
* However, the presence of an odor could be characteristic for the drug (vitamins), added ingredients (flavoring agents) or the dosage form (film-coated tablets).

**Taste:**

* Taste is important in consumer acceptance of, especially, chewable tablets.

Quality Control Tests:

1. **HARDNESS (CRUSHING STRENGTH):**
   * Tablets require a certain amount of strength, or hardness to withstand mechanical shocks of handling in manufacture, packaging and shipping.
   * Recently, the relationship of hardness to tablet disintegration and the drug dissolution (release) rate has become apparent.
   * Tablet hardness has been **defined as** the force required to break a tablet in a diametric compression test.
   * **To perform this test**, a tablet is placed between two anvils and the crushing strength that just causes the tablet to break is recorded.
   * Several **devices** operating in this manner have been used to test tablet hardness, e.g., the Erweka hardness tester.
   * ***The hardness of a tablet is a function of:***
   * The die fill and compression force (at a constant die fill, the hardness value increases and thickness decreases as additional compressive force is applied. However, at a constant compression force, hardness increases with increasing die fills and decreases with lower die fills).
   * The method of granulation (wet granulation ----- harder tablets).
   * The tablet diameter (size) ------- larger tablets require a greater force to cause fracture and are therefore, harder than smaller tablets.
   * **Hardness determinations are made throughout the tablet runs** to determine the need for pressure adjustments on the tabletting machine. If the tablet is too hard, it may not disintegrate in the require period of time to meet the dissolution specifications, and if it is too soft, it will not withstand the handling, packaging and shipping operations.
   * Tablet hardness is not an absolute indication of strength, since some formulations, when compressed into very hard tablets, tend to **‘cap’** on attrition, losing their crown portions. Therefore, another measure of tablet’s strength, its friability, is often measured.

**Method:**

Carry out the test on the batch of tablets provided using Erweka hardness tester. Calculate the mean crushing strength of 10 tablets (taken randomly).

N.B., a crushing strength of **4-8 Kg** for uncoated tablets is acceptable.

1. **friability test:**

* tablets that tend to powder, chip, and fragment when handled **lack elegance and consumer acceptance,** and can **create excessively dirty processes** in such areas of manufacturing as coating and packaging. They can also add to tablet’s **weight variation or content uniformity problems**.
* The measurement of friability is made by **Roche friabilator**. A number of tablets are weighed and placed in the tumbling apparatus where they are exposed to rolling and operated shocks resulting from free falls within the apparatus. After a given number of rotations, the tablets are weighed and the loss in weight indicates the ability of the tablets to withstand this type of wear.

**Method:**

1. Select 20 tablets randomly, dedust and weigh (WO).
2. Place the tablets in the Roche friabilator drum, switch on the apparatus adjusting the timer at 4 min. and the speed at 25 rpm.
3. At the end of this operation, remove the tablets from the friabilator, dedust and reweigh (W). (Any tablet that breaks up should be rejected before reweighing).
4. friability is expressed as a percentage loss in weight: i.e.,

***% loss = ***

**N.B.,** if the value of friability (% loss) is less than or equal to 1%, the batch is accepted.

**3-DISINTEGRATION TEST:**

* + **Disintegration** is a process in which tablets are break up into granules or smaller particles. The time it takes a tablet to disintegrate is measured in a device described in the USP/NF.
  + So, **disintegration test is** a measure of the time required for a group of tablets to break up into particles under a given set of conditions.
  + This test is **essential for** tablets intended for administration by mouth, **except** those intended to be chewed before being swallowed or those that should dissolve slowly in the mouth, e.g., lozenges, glyceryl trinitrate, or effervescent tablets. Also, disintegration does not apply to some types of sustained-release tablets.

***The USP disintegration apparatus:***

* + - This apparatus consists of a basket rack containing 6-open-ended glass tubes held in a vertical position. A number 10-mesh stainless steel wire screen is attached to the bottom.
    - To test for disintegration time, one tablet is placed in each tube and the basket rack is positioned in a 1-L beaker of water, simulated gastric fluid (pH 1.2), or simulated intestinal fluid (pH 7.4), at 37 oC. A standard motor driven device is used to move the basket assembly containing the tablets up and down through a distance of 5 to 6 cm at a frequency of 23 to 32 cycles per minute.
    - N.B., perforated discs may also be used in the test. These are placed on the top of the tablets and impart an abrasive action to the tablets. These discs are useful for tablets that float.
    - To be in compliance with the USP standards, the tablets must disintegrate, and all of the particles must pass through the 10-mesh screen in the time specified.
    - **Limit:**
    - **Uncoated USP tablets** have disintegration time standards as low as 5 minutes (aspirin tablets), but the majority of tablets have maximum disintegration time of 30 minutes.
    - **Enteric coated tablets** are to show no evidence of disintegration after 1 hour in simulated gastric fluid. These tablets are then tested in simulated intestinal fluid and are to disintegrate in 2 hours plus the time specified in the monograph.
    - **N.B.,** if one tablet fails to disintegrate within 30 minutes, the disintegration test is repeated on 12 additional tablets. Not less than 16 out oh the total 18 tablets tested disintegrate completely within 30 minutes.

**Method:**

1. Place one tablet in each of the six tubes of the basket (tablets are selected randomly).
2. Position the basket rack in 1- L beaker containing distilled water (as the disintegration medium) maintained at 37 oC.
3. Start the apparatus (to move the basket assembly containing the tablets), and record the time required for all of the six tablets to break into particles and to pass to the disintegration medium.

**Limit:**

* + The tablets should disintegrate within 30 minutes (uncoated tablets).
  + If one tablet fails to disintegrate within 30 minutes, the disintegration test is repeated on 12 additional tablets. Not less than 16 out oh the total 18 tablets tested disintegrate completely within 30 minutes.

**4-WEIGHT VARIATION TEST:**

* + - * The weight of the tablets being made should be routinely measured to help ensure that the tablet contains the proper amount of drug.
      * In practice, composite sample of tablets (usually 20) are taken and weighed throughout the compression process, the average weight is then calculated which will have the usual problems of averaged values. Within the composite sample which has an acceptable average weight, there could be tablets excessively overweight or underweight.
      * To help to alleviate this problem, the USP / NF provides limits for the permissible variations in the weights of individual tablets expressed as a % of the average weight of the sample.
      * **The USP weight variation test** is run by weighing 20 tablets individually, calculating the average weight, and comparing the individual tablet weights to the average.
      * **Limit:** the tablets meet the USP test if not more than 2 tablets are outside the % limit and if no tablet differs by more than double that percentage limit.
      * The weight variation tolerances for uncoated tablets differ depending on average tablet weight. (See the next table)

***Table: Weight variation tolerances for uncoated tablets:***

|  |  |
| --- | --- |
| Average weight of tablets (mg) | Maximum % difference allowed |
| 130 or less | ± 10 |
| 130 – 324 | ± 7.5 |
| More than 324 | ± 5 |

* **N.B.,** the weight variation test would be a satisfactory method of determining the drug content uniformity of tablets if the active ingredient is 90 to 95% of the total tablet weight. However, this test is not sufficient to assure uniform potency of tablets of moderate – or low-dose drugs, in which excipients make up the bulk of the tablet weight.

**Method:**

1. Select 20 tablets randomly from the batch provided, then weigh the tablets individually.
2. Weigh the 20 tablets together and calculate the average weight (W).
3. Compare the average weight calculated to the previous table to determine the maximum % difference allowed.
4. calculate the upper and lower limits at the % difference allowed:

Upper limit = W + [(%/100) (W)]

Lower limit = W – [(%/100) (W)]

1. Furthermore, calculate the upper and lower limits at double the % difference allowed:

Upper limit = W + [(2x %/100) (W)]

Lower limit = W – [(2x % /100) (W)]

1. Compare the individual weights of tablets to the upper and lower limits calculated at the % difference allowed and at double that percentage.
2. Comment on the results.

**Limit:**

For the batch to be accepted:

1. Not more than 2 tablets (out of the 20 tablets) differ from the average weight by the % difference listed, and
2. No tablet differs from the average weight by double that percentage.

**5- DRUG CONTENT:**

The potency (drug content) of tablet is expressed in terms of gm, mg, or mcg (for some potent drugs) of drug per tablet and is given as the label strength of the product.

**Range:**

Official compendia or other standards provide an acceptable potency range around the label potency.

* For highly potent, low-dose drugs such as digitoxin, this range is usually not less than 90% and not more than 110% of the labeled amount.
* For most other larger – dose drugs in tablet form, the official potency range that is permitted is not less than 95% and not more than 105% of the labeled amount.

**Analytical methods:**

In general, official potency analytical methods require that a composite sample of tablets be taken, ground up, mixed, and analyzed to produce an average potency value.

Even though, the average assay result looks acceptable, it could mask wide variation in potency, with the result that a patient could be variably under dosed or overdosed. With such a drug as digitoxin, in which the effective and toxic levels are close, exceeding the official or acceptable potency range is not only undesirable, but possibly dangerous.

**Three factors that can directly contribute to content uniformity problems in tablets:**

1. Non-uniform distribution of the drug throughout the powder mixture or granulation.
2. Segregation (demixing) of powder mixture or granulation during the various manufacturing processes.
3. Tablet weight variation.

**N.B.,** the use of weight cannot be used as a potency indicator except when the active ingredient is 90-95% of the total tablet weight. In tablet with smaller dosages, a good weight variation does not ensure good content uniformity, but a large weight variation precludes good content uniformity.